"I would have everie man write what he knowes and no more."—MONTAIGNE

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EDITORIAL

IN the days before mechanical means of artificial respiration were at hand in operating theatres we regarded the failure of respiration as a serious matter needing prompt attention; today the anaesthetist thinks that he can breathe for the patient so much better than the patient can breathe for himself that he deliberately depresses respiration, sometimes to the point of paralysis, and regards artificial respiration as part of the normal procedure. Serious as was the situation when respiration failed it became desperate when the heart followed suit, no radial pulse no carotid, and the surgeon in a voice pregnant with admonition would inform us that the aorta had ceased to function. The coroner told the relatives that all the usual measures to save life were put into operation at once but unfortunately without avail. Now Dr. Michael Johnstone, in the remarkable paper which we publish in this issue, tells us that quite a number of patients in whom no pulse can be felt and who to the observer appear to be dead are, in fact alive, and if the "usual measures to save life" are *not* applied will come safely through the operation. How, then, shall we distinguish between the pulseless who are dead and those who are not? Dr. Johnstone tells us that in a number of these patients the heart is at this moment of apparent death producing an electrocardiogram, and that any ill-advised attempt at cardiac massage might have fatal consequences. In addition to distinguishing the living from the dead, the electrocardiogram to the expert can tell of approaching heart failure and so put him in a position to avert it. Dr. Johnstone describes six different mechanisms of heart failure and offers a satisfying explanation of the age-old controversy between those who believed in vagal inhibition as the only cause of heart failure and those who attributed this role to ventricular fibrillation. This very important paper demonstrates the need that every operating theatre should be fitted with an electrocardiograph and that every anaesthetist should be an expert in reading electrocardiograms and familiar with the changes that occur in them signalling the imminence of impending heart failure.

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SOME MECHANISMS OF CARDIAC ARREST DURING ANAESTHESIA

BY

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THE advent of thoracic surgery has been followed by a renewal of interest in the mechanisms and treatments of the acute cardiac catastrophes which may occur during clinical anaesthesia. It has now become apparent that the cessation of cardiodynamics during anaesthesia may be due either to ventricular fibrillation or to asystole unpreceded by fibrillary phenomena. Numerous authors have acclaimed the success of direct cardiac message, and other manoeuvres, in the treatment of cardiac arrest during thoracic surgery; some have even gone so far as to advise immediate diagnostic thoracotomy when the peripheral pulse ceases to be palpable in the anaesthetized patient (Rao *et al.*, 1954; Milstein and Brock, 1954; Mullens, 1955).

It is obvious that direct cardiac massage is the only treatment for an established cardiac arrest. This treatment can be instituted promptly and with comparative ease in patients undergoing or about to undergo thoracic surgery. It should be remembered, however, that most cardiac arrests under anaesthesia occur in patients prepared for other types of surgical operations; under these circumstances the accurate diagnosis of asystole or ventricular fibrillation may be virtually impossible in the absence of cardiographic tracings. In my experience the absence of a peripheral pulse is certainly not always an indication for immediate thoracotomy to determine the state of the myocardium. Therefore, in an attempt to counter the possible overenthusiastic acceptance of cardiac massage in the treatment of cardiovascular collapse during anaesthesia, it is proposed to demonstrate that it may be possible, with the more liberal use of the electrocardiograph, to anticipate major cardiac upsets in the anaesthetized patient and to take steps to avoid their occurrence.

Many reports of animal experiments have thrown some light on the problem, but the results are controversial. It will be clear to those of us engaged in the practice of clinical anaesthesia that the final solution must inevitably be found through the medium of comprehensive clinical observation. It is doubtful whether the complex pathological and metabolic abnormalities which we regularly encounter in our everyday work will ever be reproduced in the experimental animal.

The first investigation into the aetiology of cardiovascular collapse during anaesthesia was reported by John Snow in 1858. He observed that most catastrophes occurred in the inductive phases of anaesthesia and appeared to be directly related to the inhalation of excessively high concentrations of the vapour. Cardiac inhibition could be prevented by restricting the vapour concentration to 2 per cent or less; the inhalation of higher concentrations often caused stoppage of the heart before the cessation of respiration. Snow's work was repeatedly confirmed (Kirk, 1893; Brodie and Russell, 1900; Embley, 1902). It was demonstrated that the inhalation of chloroform vapour caused reflex inhibition of the dog's heart as the result of chemical stimulation of vagal receptors in the air passages. Brodie and Russell (1900) made the important observation that, whereas stimulation of the peripheral end of the cut vagus seldom if ever caused permanent arrest of the heart, stimulation of the pulmonary branches of the vagus produced intense cardiac inhibition; they confirmed and extended the work of Snow and showed that chemical stimulation of vagal receptors in the lower air passages caused reflex arrest of the heart.

Levy (1912), using the electrocardiograph for the first time in experimental anaesthesia, emphasized his belief that chloroform syncope in cats was due to an hyperexcitability of the ventricles leading to ventricular tachycardia and ventricular fibrillation. This hyperexcitability of the ventricles

was associated with overactivity of the sympathetic nervous system. He was very critical of the views of Snow and his supporters and refused to accept that the vagus played any part in the suppression of the heartbeat during anaesthesia. In the following years Levy's thesis was generally accepted and the vagal concept tended to be overlooked. It is not improbable that the principal reason for the general acceptance of Levy's work was the fact that his descriptions were supported by indisputably accurate cardiograms.

More recently, Sealy *et al.* (1954) and Young *et al.* (1954) disputed the suggestions that autonomic activity played any part in cardiovascular collapse during anaesthesia. They demonstrated that retention of carbon dioxide during anaesthesia in animals caused a rise in the plasma potassium to cardiotoxic levels. A sudden lowering of the alveolar CO_2 level, after a prolonged period of hypercarbia, was followed by a still further increase in the plasma potassium content which precipitated fatal ventricular fibrillation. They made the important observation that electrocardiographic changes were the only important signs of impending cardiovascular collapse; these changes occurred sufficiently early to permit the institution of successful corrective measures.

These three theories—the vagal concept of the earlier workers, the sympathetic hyperirritability of Levy, and the potassium intoxication of Sealy—represent our knowledge of the factors which predispose to sudden cardiac arrest during anaesthesia in animals. I have no doubt that the findings of these three groups of workers are perfectly correct but I hope to show that the criticisms of the latter groups were unjustifiable. I feel quite certain that sudden cardiovascular collapse during clinical anaesthesia may be due to any one of the three mechanisms described, in addition to others not yet fully understood.

During the past eight years I have made extensive use of the electrocardiograph during clinical anaesthesia in all types of patients undergoing major and minor surgical procedures. It has now become apparent that there are at least five different and clearly defined sequences of cardiac derangement which may occur in man and which may lead to complete arrest of the heart. The object of the present paper is to present a series of case reports, complete with cardiograms, illustrating some of the changes of cardiac action which may end in arrest. I will endeavour to show that autonomic overactivity of either the sympathetic or parasympathetic nervous systems, potassium intoxication, and interference with the coronary circulation, produce specific electrocardiographic changes which, if identified in the early stages, may provide sufficient warning of impending arrest to permit the early application of successful resuscitative measures.

Arrest by Vagal Overactivity.

This is the mechanism first identified by Snow but later denied by many workers because they were unable to cause permanent arrest of the animal heart by stimulation of the peripheral end of the cut vagus. I think that these workers were unwise in assuming that the cardiac effects induced by stimulation of the peripheral end of the cut vagus were necessarily similar to those induced reflexly—with irritant anaesthetic vapours—of the innumerable vagal receptors situated in the air passages. Furthermore, we cannot deny the possibility of vagal arrest of the human heart simply because it is impossible to stop an animal's heart by direct vagal stimulation. We should remember that the human autonomic nervous system is subject to variations of activity which do not obtain in animals—variations which seem to be related to conditions such as peptic ulceration, essential hypertension, certain forms of cardiac arrhythmia, bronchial asthma, and other states now referred to as syndromes of adaptation or stress.

By the simple experiment of filling the lungs with a mixture of gases containing an irritant vapour, and at the same time preventing coughing and straining (Johnstone, 1951a; 1953b), it is possible in some individuals to induce a condition which simulates death so closely as to be indistinguishable from it clinically and electrocardiographically, especially in curarized subjects. The following case illustrates this mechanism.

CASE 1

Healthy male, 41 years. Herniorrhaphy. No preoperative drugs given. Anaesthesia induced with thiopentone and maintained smoothly for fifteen minutes with nitrous oxide, oxygen, and trichlorethylene. Ether was then added and respiration assisted. A few minutes later the patient became profoundly collapsed and pulseless; the cardiograph revealed cardiac arrest (fig. 1, D). During the period of arrest the respiratory movements were shallow and gasping. The ether and

trichlorethylene were immediately turned off and the patient ventilated with oxygen; three minutes later the cardiovascular system had returned to normal and the patient made an uneventful recovery. The electrocardiographic details of the case are illustrated on figure 1.

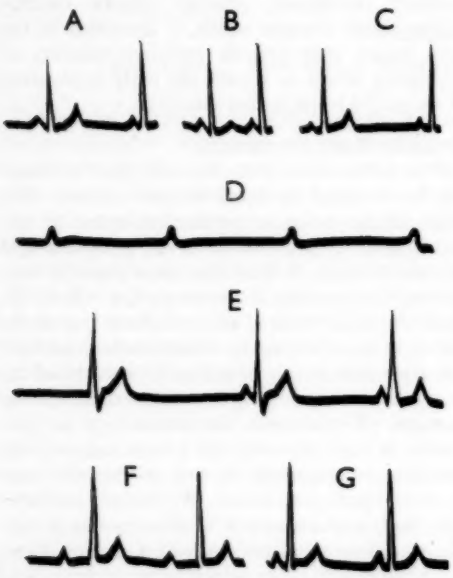

FIG. 1

Male, 41 years. All Lead 2.

A. Before induction. Sinus rhythm 60/minute.
B. After thiopentone induction. Sinus rhythm 120/minute.
C. Trichlorethylene anaesthesia for fifteen minutes. Sinus rhythm 50/minute.
D. Ether added six minutes previously and respiration assisted. Patient apparently dead. Complete atrioventricular block with ventricular standstill.
E. Thirty seconds after removal of the mask. Aberrant supraventricular complexes appear.
F. Two minutes later. Sinus rhythm 60/minute.
G. Three minutes later.

By courtesy of the *British Heart Journal* (1951), **13**, 47.

I cannot say whether a cardiac arrest induced in this manner can be permanent, but, when one reads the published reports of fatal arrests during anaesthesia, I feel that it is reasonable to assume that this mechanism was involved in some of them. It has been shown that small doses of pethidine (Johnstone, 1951b) and of morphine (Embley, 1902; Cohn, 1913) may increase the sensitivity of vagal reflexes and, thereby, predispose to cardiac arrest when irritant vapours are inhaled. The muscarinic action of neostigmine and of suxamethonium (Johnstone, 1955) may precipitate vagal cardiovascular collapse in sensitive patients unprotected by atropine.

This type of arrest should be regarded as an ever-present risk when anaesthesia is induced or maintained with ether, ethyl chloride, chloroform, cyclopropane, and trichlorethylene. It may also occur when the pulmonary branches of the vagus are stimulated by surgical manipulations (O'Shaugnessy, 1936; Edwards, 1938). The transition from normal pulse rate to complete arrest requires one or two minutes, depending on the intensity of stimulation. I suspect that cyanotic pallor and cessation of respiration are relatively late signs of cardiac arrest of this type. Normal cardiac function can be restored either by withdrawing the irritant vapour and ventilating with nitrous oxide and oxygen, or by administering atropine intravenously. Atropine—0.5 mg to 1.0 mg—will prevent or abolish this type of cardiac inhibition and is at present the only known antidote. Judging from the few cases of complete vagal arrest of the heart which I have observed during clinical anaesthesia I think that spontaneous recovery of the heart is possible after sixty seconds complete stoppage, providing the precipitating agent is promptly removed. Atropine, administered by intravenous injection, reaches its peak vagolytic effect in twenty or thirty seconds. During electrocardiographic observations on many hundreds of patients I have never seen any suggestion of active potentiation of vagal activity following the intravenous administration of the drug. I am not aware of any effort to determine whether other vagolytics, with the exception of gallamine triethiodide (Johnstone, 1955), are suitable substitutes for atropine in this respect. Pethidine, which is known to have a weak atropine-like effect in animals (Eisleb and Schaumann, 1939), provides no protection against reflex cardiac inhibition; it appears to increase the sensitivity of the pulmocardiac reflex by preventing bronchiolar constriction when the irritant vapours are inhaled (Johnstone, 1951b). The use of intravenous barbiturates and nitrous oxide mixtures for the induction and maintenance of anaesthesia completely eliminates the risk of this type of arrest

during anaesthesia in all cases except those involving surgical stimulation of the vagus nerve and its pulmonary branches.

The Ventricular Tachycardia—Fibrillation Sequence.

This is the disturbance first observed by Oliver and Schafer (1895) and later confirmed electrocardiographically by Levy (1912). It has repeatedly been shown to be caused by overactivity of the sympathetic nervous system (Elliott, 1912; Bathia and Burn, 1933; Cattell, 1923; Allen *et al.*, 1940), and occurs classically when an overdose of adrenaline or noradrenaline is administered to an anaesthetized subject. It is interesting to note that Snow (1858) drew attention to the fact that sudden and unexpected death was not an uncommon occurrence in the early stages of surgical operations in the pre-anaesthetic days; Levine (1952) observed that acute fear has precipitated ventricular tachycardia in a susceptible patient.

The induction of anaesthesia with agents such as chloroform, ether, cyclopropane, and trichlorethylene, which have repeatedly been shown to increase the secretion of adrenaline, is often associated with the appearance of severe cardiac arrhythmias, especially in nervous or excited patients. The cardiac disturbance consists of a rapidly progressive increase in the sinus rate, increase in the amplitudes of the P and T waves, the appearance of ventricular extrasystoles which gradually increase in frequency till they completely dominate the cardiac rhythm; in fatal cases the extrasystolic beats are soon followed by ventricular fibrillation. A similar sequence of events may be observed when carbon dioxide retention is allowed to occur during the maintenance of anaesthesia with cyclopropane, chloroform, trichlorethylene, thiopentone, and most other agents. More detailed descriptions of the aetiology and control of these arrhythmias have already been published (Johnstone, 1950 *et seq.*).

I have now come to regard the occurrence of extrasystolic beats during anaesthesia as an indication that ventilation, whether spontaneous or controlled, is inefficient and has permitted the retention of carbon dioxide; this applies to anaesthesia with all agents, including cyclopropane and trichlorethylene. The use of the thiopentone—nitrous oxide—oxygen—curare sequence does not in any way predispose to the more severe degrees of ventricular arrhythmias, though occasional extrasystoles and bigeminy may be observed when the elimination of carbon dioxide is inadequate. The only other circumstances in which I have observed these arrhythmias are during surgical manipulation of the heart and after the administration of sympathetic stimulants to anaesthetized patients.

I have been unable to observe that oxygen lack plays any part in their production, and reliable evidence seems to indicate that it may prevent their appearance (Harris, 1946; Zeigler, 1948). Levy (1913) observed that asphyxia and deep anaesthesia protected the animal heart from the effects of adrenaline administered during chloroform anaesthesia. He also noted that spontaneous cardiac irregularities were less likely to occur during chloroform anaesthesia when the systolic pressure was less than 100 mm Hg, or when artificial respiration was performed. After prolonged deep anaesthesia in man, or in the presence of surgical shock, carbon dioxide retention has not the same tendency to cause cardiac arrhythmias during cyclopropane or trichlorethylene anaesthesia. It is now well established that procaine will abolish ectopic cardiac rhythms through its depressant effect on the conducting mechanisms (M'Clendon *et al.*, 1951). It would appear, therefore, that the appearance of ectopic disturbances during anaesthesia indicates the effects of excessive adrenaline on the intact Purkinje cells. When the activity of these cells is depressed by deep anaesthesia, procaine, vascular hypotension, or hypoxia, the irritability of the ectopic centres of impulse formation is correspondingly depressed. If the depression of these cells is excessive or prolonged, the sino-atrial and the atrioventricular nodes may cease to function. It is also possible, however, that the depression of cardiac irritability by the above mentioned factors may be related to suppression of the sympathetic and adrenal activity.

An important feature of the extrasystolic arrhythmias is that they can be abolished by stimulation of the vagal pulmocardiac reflex in the manner described in the previous section. The insufflation of ether vapour provides a convenient method for doing this and is most effective in dealing with the severe arrhythmias which

may be precipitated by the administration of adrenaline or noradrenaline during anaesthesia (Johnstone, 1953a). Conversely, in the presence of increased sympathetic activity, the sudden abolition of vagal function by vagolytic drugs such as atropine or gallamine may release the ectopic centres of impulse formation normally held in restraint by the inhibitory effect of the vagus (Levy, 1912; Johnstone, 1951a, 1955).

Recognition of the disturbance of cardiac rhythm due to sympathetic overactivity is difficult without the aid of an electrocardiograph. It is doubtful whether multifocal ventricular tachycardia can be accurately recognized by inspection of the exposed heart. Levy (1912) emphasized that multifocal ventricular tachycardia was indistinguishable from the coarse type of ventricular fibrillation except by electrocardiographic methods. This point should be carefully considered when assessing the merits of the treatment of cardiac derangements diagnosed by direct inspection of the heart. Ventricular tachycardia is certainly not an indication for cardiac massage as it can be remedied by more conservative means. Ventricular fibrillation, on the other hand, indicates a seriously damaged myocardium which may require assistance by massage.

Cardiac Disturbances due to Electrolytic Imbalance.

Since the estimation of the blood electrolytes was facilitated by the introduction of the flame photometer (Barnes *et al.*, 1945) it has become more obvious that the electrolytes play an important part in the maintenance of cardiovascular efficiency during anaesthesia and surgery. The sodium, potassium, and chloride ions have received most of the attention, and of these potassium is the most interesting from the anaesthetist's point of view. It is now generally accepted that potassium excess (Marchand and Finch, 1944) or potassium deficiency (Lewis *et al.*, 1954; McAllen, 1955) may lead to severe cardiovascular collapse. The effects of anaesthesia on the patient with potassium deficiency have not yet been clearly defined. There are, undoubtedly, aspects of potassium deficiency which are of much importance in relation to relaxant drugs and somatic myoneural function; this matter is at present under consideration and the evidence is incomplete. Potassium intoxication is encountered less frequently than deficiency but is liable to have more serious consequences.

The potassium ion is normally present in relatively high proportions in the intracellular spaces. Under certain conditions, such as metabolic acidosis and glycogenolysis (Mudge, 1953; Keating *et al.*, 1953), respiratory acidosis (Cattell and Civin, 1938; Abrams *et al.*, 1951), or after the administration of adrenaline (D'Silva, 1936; Lamson and Greig, 1953), it moves from the intracellular to the extracellular spaces with the result that the level in the plasma rises. A similar rise may follow excessive intake of potassium. In the presence of any renal function the rise in plasma potassium is dealt with immediately by an increased excretion of potassium in the urine. When kidney function has been stopped, however, by conditions such as calculus anuria, obstruction of both ureters, pyelonephritis, glomerulonephritis, or severe systemic infections, a progressive rise occurs in the level of the plasma potassium and results in ventricular fibrillation. The sequence of electrocardiographic changes associated with potassium intoxication is diagnostic of the condition (Hoff *et al.*, 1941), consisting of:

(1) Increase in the amplitude of the T wave which loses its normal rounded contour and becomes pointed.
(2) The S wave becomes deeper and wider.
(3) The P wave disappears.
(4) The widening of the ventricular deflection progresses gradually to complete disorganization of the complex with the appearance of ventricular fibrillation.

Several of these changes are illustrated in the following case.

CASE 2

Male, 39 years. Oliguria for 14 days, with anuria for the previous 48 hours. Six months history of backache. Heart, lungs, and abdomen appear normal. Blood pressure 150/90 mm Hg, blood urea 247 mg per cent, haemoglobin 9 g per cent. For cystoscopy and retrograde catheterization of the ureters. Premedication atropine 0.5 mg. General anaesthesia considered suitable because of some restlessness and mental confusion. An electrocardiogram taken immediately before induction revealed signs suggestive of potassium intoxication of the heart (fig. 2, A).

Anaesthesia was induced with thiopentone 200 mg injected intravenously, followed by suxamethonium 50 mg as soon as the patient was asleep. Apnoea followed the injection of these drugs. After about fifteen

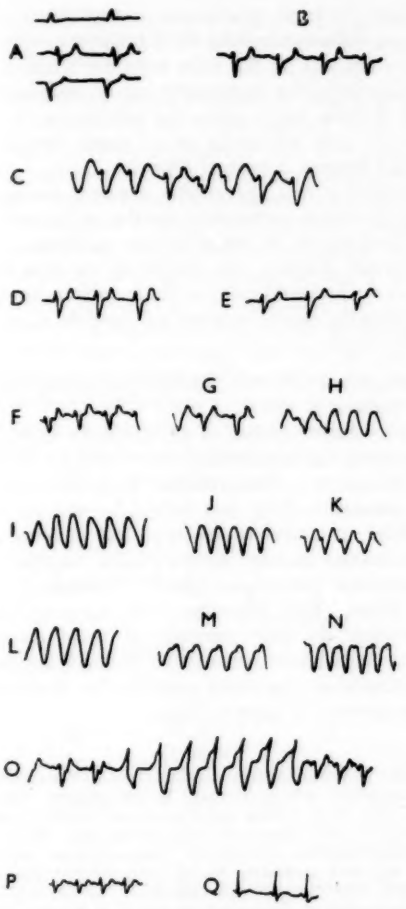

FIG. 2

Male, 39 years. All tracings, except A, are Lead 2.

A. Before induction. Leads 1, 2, and 3. Large tented T2 and T3.
B. After thiopentone induction.
C. After suxamethonium and fifteen seconds apnoea.
D. Thirty seconds later, efficiently ventilated.
E. After twenty minutes anaesthesia.
F. Thirty seconds later, carbon dioxide started.
G. One minute later.
H. Five minutes later, immediately before the injection of procaine hydrochloride.
I. Two minutes after the procaine injection.
J. Fifteen minutes later.
K. Two hours after the induction of anaesthesia.
L. Two minutes later, after the injection of procaine amide.

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seconds of complete apnoea it was noticed that the P waves of the cardiogram had disappeared, the QRS became wider and deeper, and the amplitude of the T wave increased (fig. 2, C). An endotracheal tube was promptly inserted and the patient efficiently ventilated with nitrous oxide and oxygen; the cardiogram returned to its pre-operative appearance within thirty seconds (fig. 2, D). Brisk spontaneous respiration returned in two or three minutes and both ureters were successfully catheterized in twenty minutes. During this time a further 100 mg of thiopentone and 50 mg of suxamethonium were administered intravenously without causing any electrocardiographic changes.

At the end of the operation it was decided to administer some carbon dioxide to augment the respiratory movements which were depressed by overventilation. Carbon dioxide 20 per cent in oxygen was given for thirty seconds and caused a brisk increase in the respiratory movements. Coincident with the onset of respiratory stimulation, changes occurred in the cardiogram similar to those seen after induction. These changes progressed rapidly to what appeared to be ventricular flutter or fibrillation (fig. 2, H), in spite of efficient ventilation. At times it was thought that a very feeble pulse could be felt in the carotid arteries, though none could be felt in the radial artery. Respiration remained brisk, rather like that associated with hypoxic stimulation of the respiratory centre. Ten minutes later the patient became restless and removed his endotracheal tube. A blood sample, taken immediately after the collapse at the end of the operation, later revealed the serum potassium to be 9.35 m equiv./litre (36 mg per cent).

After twenty minutes, during which time his respiration was brisk and the cardiovascular system unchanged, 4 ml of 1 per cent procaine hydrochloride were injected intravenously; this caused further deterioration of the cardiogram (fig. 2, I), the peripheral pulse disappeared completely, and restlessness ceased. Fifteen minutes later there was a slight improvement in the cardiogram (fig. 2, J) and some restlessness returned. One hour later (fig. 2, K) there was no appreciable change in the patient's condition and it was decided to give procaine amide; 500 mg were injected intravenously over a period of five minutes and caused deterioration similar to that caused by procaine hydrochloride (fig. 2, L). Thirty minutes later 100 ml of 50 per cent glucose solution with 50 units of insulin were injected intravenously and caused little change in the patient's condition (fig. 2, M). One and a half hours later (fig. 2, N), when it was felt that the patient was dying, it was decided to repeat the glucose-insulin therapy and a similar dose was again administered intravenously. Within five minutes of the completion of the injection, which was four hours after the onset of the collapse, a sudden and dramatic improve-

M. Ten minutes later, after the first glucose-insulin therapy.
N. Four hours after the induction of anaesthesia, and immediately before the second glucose-insulin therapy.
O. Five minutes later.
P. Ten minutes later.
Q. Three days later, serum potassium within normal limits.

ment occurred in both the clinical and electrocardiographic states of the patient: he became fully conscious and the cardiogram reverted to its pre-operative appearance (fig. 2, P); the serum potassium at this time had dropped to 8.05 m equiv./litre (31 mg per cent). The improvement was maintained and ion-exchange resins restored the serum potassium to normal levels in three days (fig. 2, Q).

The patient passed urine normally for a few days after the catheterization of the ureters, his blood chemistry and cardiovascular system becoming quite normal. Anuria then returned, apparently due to obstruction of the ureters by a retroperitoneal tumor. Bilateral nephrostomies were made, one under spinal anaesthesia and one under general anaesthesia, without complication. One month later the presence of an inoperable retroperitoneal tumor was confirmed by laparotomy; this operation was performed under general anaesthesia and was not associated with any cardiovascular disturbance as his plasma potassium was within normal limits. At the present time, which is over twelve months after the original cystoscopy, the patient is active and ambulant.

This case illustrates several interesting points. Firstly, it shows how the cardiac effects of potassium intoxication can be dangerously intensified by respiratory acidosis induced by endogenous or by exogenous carbon dioxide. Secondly, the effectiveness of the glucose-insulin therapy of potassium intoxication (Seldin and Tarail, 1949; Merrill *et al.*, 1950) has been demonstrated. Thirdly, it illustrates the need for accurate observation of the sequence of events which precede the onset of serious electrocardiographic disturbances during anaesthesia. Inspection of tracings figure 2, C and K, might give the impression that a ventricular tachycardia was present; however, having seen on the oscilloscope that the abnormality was preceded by a progressive widening of the QRS complex associated with a deepening of the S wave, elevation of the T wave, and disappearance of the P wave, one can better describe the cardiogram as illustrating a diffuse intraventricular block: this is a condition fundamentally different from ventricular tachycardia.

It is generally accepted that ventricular tachycardia, as it occurs during anaesthesia, is due to a hyperexcitability of the Purkinje network and is not in any way related to blockade or depression of the specialized tissue such as occurs in potassium intoxication (Winkler *et al.*, 1938; Winkler and Hoff, 1943). The onset of ventricular tachycardia is preceded by a characteristic sequence of changes: the amplitude of the P wave increases, the QRS and PR intervals generally become smaller, isolated ventricular extrasystoles then appear, followed rapidly by bigeminy (coupling), and eventually all the sinus beats are replaced by extrasystoles; the arrhythmia can be abolished at any of these stages either by eliminating carbon dioxide more efficiently, or by vagal stimulation in the manner described above.

Realizing that the cardiac changes associated with potassium intoxication are due to impairment of conduction in the Purkinje network, it is obviously illogical and dangerous to treat with procaine hydrochloride or amide which can only increase the degree of block still further, as shown in this case.

Spontaneous Coronary Thrombosis during Anaesthesia.

Obliterative disease of the coronary arteries is becoming an increasingly more frequent finding in pre-operative examinations. Its precise relation to anaesthetic drugs and techniques has not been defined. It is obvious, however, that patients with this disease usually survive major surgical and anaesthetic procedures without myocardial deterioration. The following case history, which describes the only example of acute coronary thrombosis I have encountered during anaesthesia, illustrates an important point in the anaesthetic management of such patients.

CASE 3

Male, 63 years. Severe angina of effort. No oedema or cyanosis. Lungs normal. Blood pressure 140/100 mm Hg. Left stellate ganglionectomy twelve months previously with transient relief from pain. For transthoracic cardiac neurectomy. Premedication atropine 0.5 mg with pethidine 50 mg administered subcutaneously one hour before operation. Quite calm and without pain or discomfort on arrival at theatre. Blood pressure and cardiogram unchanged (fig. 3, A). Anaesthesia was induced with 250 mg of thiopentone injected intravenously, followed by suxamethonium 50 mg and endotracheal intubation. There were no significant changes in the cardiogram following induction and intubation (fig. 3, B). Three minutes later the effects of suxamethonium disappeared and the patient began to cough and strain on the endotracheal tube. An attempt to control the coughing and straining with a further dose of relaxant was delayed for about three minutes because of considerable difficulty in finding a suitable vein. Thirty seconds after the onset of the coughing the QRS complex of Lead 2 became smaller and the ST segment elevated (fig. 3, C); two minutes later the rate dropped to 50 beats a minute and the ST shift became more pronounced, the pulse being imperceptible at the wrist. During the next forty minutes the ventricular complex became wider, the rate slowed, and the heart eventually stopped (fig. 3, D,E,F). Cardiac

massage was performed in the early stages of the collapse but was soon abandoned as the coronary arteries felt hard and brittle.

The changes which occurred in Lead 1 in this case are interesting and might possibly prove misleading if too much emphasis were to be placed on the examination of isolated single-lead cardiograms. Prior to induction it shows a sinus rhythm with an inverted T wave. No significant changes occurred during induction and intubation. During the period of coughing, however, the T wave became erect to the normal position (fig. 3, C) and the tracing appeared to be improved although the patient was *in extremis*. This type of change illustrates the importance of having serial tracings in at least two leads when a collapse is anticipated or is being investigated. Errors of diagnosis may occur when isolated single-lead tracings are taken after the collapse has supervened.

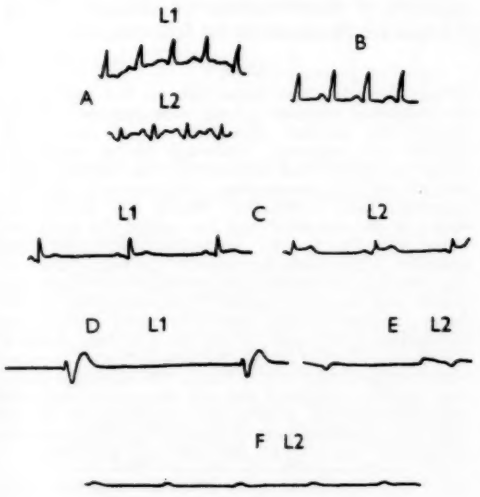

FIG. 3
Male, 63 years.

A. Leads 1 and 2, immediately before induction.
B. Lead 1, after induction and intubation.
C. Leads 1 and 2. Five minutes later, patient coughing. Note that T1 is now erect, and ST2 is considerably elevated.
D. Lead 1. Twenty minutes later, patient clinically dead.
E. Lead 2. A few minutes later.
F. Forty minutes after the induction of anaesthesia. Patient dead.

I am of the opinion that the fatal coronary occlusion in this case was precipitated by the muscular effort and partial asphyxia of coughing on the endotracheal tube. Many patients, with even more severe degrees of coronary insufficiency, have been successfully anaesthetized using similar drugs and technique, and no evidence of myocardial deterioration has been observed; coughing and straining were carefully avoided in all these cases by adequate and timely curarization.

Myocardial Ischaemia during Mitral Valvotomy.

During the operation of mitral valvotomy the cardiogram often shows signs of myocardial ischaemia for a short time immediately after the removal of the surgeon's finger from the valve orifice. Whilst the commissures of the valve are being split, a multifocal ventricular rhythm almost invariably replaces the normal supraventricular complexes (fig. 4, F, G, H); this arrhythmia appears to be due to tactile stimulation or stretching of Purkinje fibres, as its onset coincides exactly with the insertion of the finger into the valve ring and it subsides immediately after the finger is withdrawn into the cavity of the auricle—it is not necessary to withdraw the finger from the auricle to abolish the arrhythmia. When the supraventricular complexes reappear they generally show a decrease in rate and displacement of the ST segment (fig. 4, F, G, H). With each successive attempt at splitting the commissures the rate becomes slower and the ST segment more displaced until the degree of displacement may be extreme (fig. 4, I); at this stage it is impossible to feel a peripheral pulse. I think that this change in the position of the ST segment indicates myocardial ischaemia secondary to vascular obstruction at the mitral valve. The ST segment resumes its normal iso-electric position within one or two minutes after the withdrawal of the finger from the valve orifice (fig. 4, J, K, L, M). It is therefore advisable to observe the behaviour of the ST segment when several attempts at valve splitting are required. A severe degree of shift indicates the need for a pause to permit the return of the coronary circulation; neglect to observe these changes may lead to myocardial anoxia and cardiac arrest.

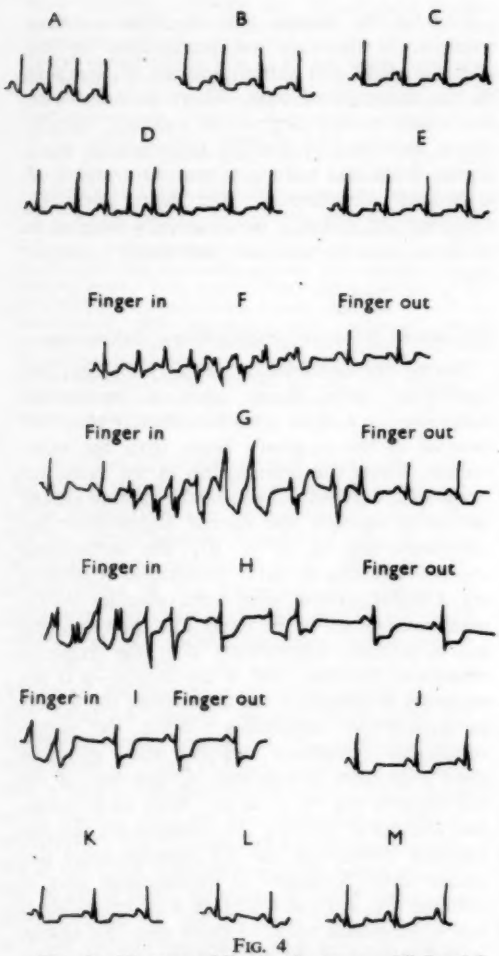

FIG. 4

Female, 32 years. Mitral valvotomy. All Lead 2.

A. Before induction.
B. After thiopentone, suxamethonium, and intubation.
C. Twenty minutes later, on nitrous oxide, oxygen, and full curarization. Chest open.
D. Auricular clamp applied. Sinus rhythm is interrupted by auricular extrasystoles.
E. Finger in the auricle. Regular sinus rhythm.
F. First attempt at valve splitting. Shows ventricular extrasystoles giving way to sinus beats when the finger is withdrawn from the valve ring.
G. Second attempt at valve splitting. Shows multifocal ventricular tachycardia giving way to sinus beats when the finger is withdrawn from the valve.

[*continued at foot of next column*

Accidental Coronary Occlusion during Cardiac Surgery.

The intimate relation of the left coronary artery to the base of the left auricular appendage is well known. This artery, and particularly its circumflex branch, is liable to compression between the anterior wall of the left ventricle and the handle of the clamp which is applied to the auricular appendage immediately before the insertion and immediately after the withdrawal of the surgeon's finger. When the clamp is reapplied after the valve has been split, the blood pressure is usually very low and the lumen of the coronary artery can be easily obliterated. A more complete description of the mechanics of this type of coronary occlusion has recently been published by Mudd *et al.* (1954).

Occlusion of a large branch of a coronary artery naturally leads to a sudden and profound collapse of the patient with a characteristic sequence of electrocardiograph changes. These changes are illustrated in the following case.

CASE 4

Female, 26 years, with mitral stenosis. For valvotomy. Premedication atropine 0.5 mg, with pethidine 50 mg. Anaesthesia induced with 200 mg of thiopentone injected intravenously, intubated during suxamethonium paralysis, and maintained with nitrous oxide, oxygen, and full curarization. The patient's condition remained very satisfactory during the preliminary stages of the operation and also whilst the valve was being split (fig. 5, A–F). Immediately after the reapplication of the auricular clamp to facilitate closure of the auricular appendage, the patient became pulseless, pallid, and faintly cyanotic; direct inspection of the heart revealed a slow and very weak contraction. Coincident to the onset of the collapse there occurred a sudden elevation of the ST segment and the sinus rate became slower (fig. 5, G,H,I). The auricular suture was rapidly completed and the clamp removed; this was followed by a dramatic improvement in the patient's condition both clinically and electrocardiographically (fig. 5, J, K). Recovery was uneventful.

H. Third attempt at valve splitting. Again a multifocal ventricular tachycardia gives way to a sinus rhythm when the finger is withdrawn. The sinus rate is now slower, the T wave deeply inverted, and the displacement of the ST segment is increasing rapidly.
I. End of fourth and successful attempt at valve splitting. There is now an extreme degree of ST shift.
J. Three minutes later, auricular sutures being inserted. The ST shift is less.
K. Five minutes later.
L. Ten minutes later.
M. Fifteen minutes later. The tracing has now reverted to its pre-operative appearance.

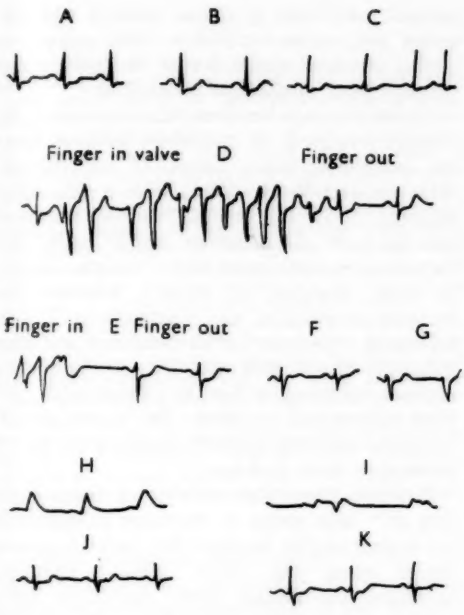

FIG. 5

Female, 26 years. Mitral valvotomy.

All tracings, except H and I, are Lead 2.

A. Before induction.
B. Twenty minutes later, chest open under nitrous oxide, oxygen, and full curarization.
C. Auricular clamp applied. Sinus rhythm interrupted by auricular extrasystoles.
D. First attempt at valve splitting. Shows multifocal ventricular tachycardia giving way to sinus rhythm when the finger is withdrawn from the valve.
E. Second and successful attempt at valve splitting. Tracing again shows a ventricular rhythm giving way to a sinus rhythm when the finger is withdrawn from the valve. The T wave is now diaphasic and the ST segment displaced.
F. One minute later. ST segment in normal position.
G. Thirty seconds later, auricular clamp *in situ*. The S wave has suddenly become wider and deeper.
H. Lead 1. Ten seconds later. Note the extreme elevation of the ST segment.
I. Lead 1. Fifteen seconds later. Patient apparently moribund.
J. Lead 2. Thirty seconds later, after the removal of the auricular clamp. ST segment and T wave normal.
K. Lead 2. Ten minutes later. Patient's condition now satisfactory.

DISCUSSION

These notes describe six sets of circumstances which may lead to complete cardiac arrest. They depict cardiac collapse due to vagal overactivity, to sympathetic overactivity, to potassium intoxication, and to acute coronary insufficiency induced in three different ways. Each type of collapse was preceded by characteristic electrocardiographic changes which provided good warning for the institution of specific resuscitative measures. In addition to these mechanisms there are others which have not been fully described: those due to asphyxia, acute haemorrhage, acute adrenocortical insufficiency (Lewis *et al.*, 1953; Galante *et al.*, 1954; Root, 1955), hypothermic fibrillation (McWilliam, 1887), obstruction of the pulmonary artery (Masson and Branwood, 1955), and others not yet identified. It is not improbable that each of these conditions in the early stages may cause a characteristic sequence of electrocardiographic changes calling for specific remedies.

In extreme cases of cardiovascular collapse the electrocardiograph may provide the only evidence of life and may save the patient from unnecessary cardiac massage, as the following case illustrates.

CASE 5

Female, 32 years. Excellent condition, with normal cardiovascular and respiratory systems. For dilatation of the cervix and curettage of the uterus. Morphia 15 mg with atropine 0.5 mg administered subcutaneously ten minutes before the induction of anaesthesia. The operation was completed uneventfully in ten minutes under thiopentone 300 mg with gallamine 40 mg injected intravenously, respiration being spontaneous throughout. On leaving the theatre the patient was asleep and in good condition. Ten minutes later, whilst awaiting transport back to the ward, she was found to be apparently dead: the face showed a waxen-cyanotic pallor, the pupils were dilated and the corneal reflex absent, there was no evidence of spontaneous respiration, no pulsation could be felt in either the radial or carotid arteries, and the heart sounds could not be heard. An electrocardiograph was attached immediately and, at the same time, a tightly fitting endotracheal tube was inserted and the lungs briskly inflated with oxygen; the pulmonary inflation was designed not only to oxygenate the lungs but rhythmically to compress the heart. The first tracing was obtained about thirty seconds after the start of pulmonary inflation and shows only one aberrant ventricular complex (fig. 6 A). Ten seconds later the aberrant beats had increased in frequency (fig. 6, B), and one and a half minutes later a bigeminal rhythm had appeared and a slow pulsation became palpable in the carotid artery (fig. 6, C). Ten minutes later the cardiovascular system was quite normal apart from a slight degree of partial atrioventricular block

(fig. 6, E). Artificial respiration was continued for a further fifty minutes before spontaneous respiration returned. Two hours later the patient was conscious and rational. No evidence of neurological sequelae was detected and recovery was uneventful.

I feel reasonably certain that virtually complete cardiac arrest had occurred in this patient as the result of asphyxia. The response to brisk pulmonary inflation was dramatic and provided clinical support for the experimental observation of Thompson *et al.* (1946) who, with the aid of radio-active sodium ions in the heparinized blood of dead dogs, demonstrated that pulmonary inflation produced a distinct circulation of the blood of the dead animals. I have also observed

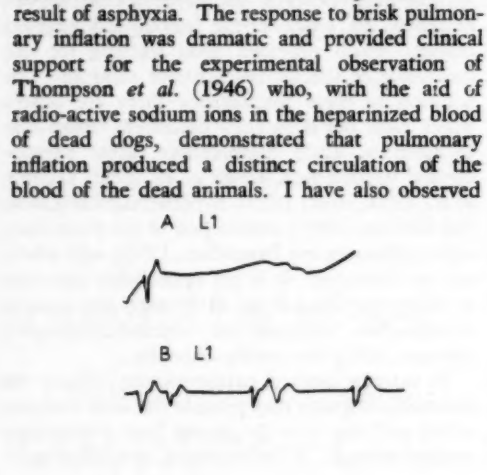

FIG. 6

Female, 32 years. Curettage of the uterus. All Lead 2.

A. Thirty seconds after the start of pulmonary inflation. Shows only one aberrant ventricular beat.
B. Ten seconds later. Aberrant beats increase in frequency.
C. After one and a half minutes of brisk pulmonary ventilation. Atrioventricular dissociation with ventricular extrasystoles coupled to the AV nodal beats. Feeble carotid pulse felt, 30 per minute.
D. Five minutes later, pulse palpable at wrist, 44 beats a minute. Atrioventricular dissociation.
E. Fifteen minutes later. Sinus rhythm, 47 beats a minute. Slight degree of atrioventricular block.

dramatic recoveries in a few children who collapsed and became pulseless after periods of intense laryngeal spasm during the induction or recovery from inhalational anaesthesia.

Cardiac massage has been recommended as the primary treatment of circulatory collapse when the peripheral pulse ceases to be palpable (Milstein and Brock, 1954; Rao *et al.*, 1954; Mullens, 1955). It is obvious that such treatment may be quite commendable and is easily performed on patients prepared for thoracic surgery. In other branches of surgery, however, the decision to perform this treatment is a most harrowing experience for all concerned and must inevitably be associated with delay in a proportion of cases, resulting, at best, in patients with crippling neurological sequelae. The instantaneously recording electrocardiograph provides the answer to many of these problems.

I cannot accept that inability to detect pulsation in a large artery is invariably an indication for prompt cardiac massage. On several occasions, whilst using the "total spinal" technique (Griffiths and Gillies, 1948) for major pelvic surgery, I have been unable, for various reasons, to feel any pulsation in the peripheral arteries; in all these cases the cardiogram has remained unaltered in the three limb leads and the patients have made uneventful recoveries without the need of resuscitation. On one occasion, whilst performing an abdominoperineal resection of the rectum under a "total spinal", the surgeon was unable to feel pulsation in the iliac arteries; in spite of this the cardiogram remained perfectly normal, the operation was completed without the need of supportive therapy, and the patient made an uneventful recovery.

Traction or pressure in the region of the coeliac plexus in some patients causes intense peripheral vasoconstriction with complete disappearance of the arterial pulse but persistence of the heart beat. Similarly, the use of excessively high or sustained intra-alveolar gas pressures during the ventilation of curarized patients may render them pulseless, yet the heart continues to beat and the cardiogram remains unaltered for a time. A further cause of pulselessness during operation was recently encountered and provides evidence of the value of continuous electrocardiography during anaesthesia.

CASE 6

Middle-aged, thin female, for exploratory laparotomy. Known to have a malignant carcinoid of the intestine with secondaries in the liver. Severe vasomotor complications, of the type described in detail by Thorson *et al.* (1954), occurred periodically as the result of a toxin (enteramine or serotonin) secreted by the tumours. During these attacks she developed a patchy cyanosis, orthopnoea of the bronchial-asthmatic type, and the peripheral arteries became quite pulseless; consciousness and the cardiogram remained relatively unaltered. Anaesthesia was induced with thiopentone 200 mg, suxamethonium 50 mg, and continued with nitrous oxide and oxygen through an orotracheal tube with controlled respiration using 15 mg of d-tubocurarine. A severe vasomotor attack commenced five minutes after induction and persisted throughout the operation which lasted forty-five minutes. During this time the patient was quite pulseless, the limbs cold and patchily cyanosed, and the lungs difficult to inflate; apart from occasional diaphragmatic twitches, the only sign of life available to the anaesthetist was the cardiogram which remained significantly unaltered throughout the operation. The peripheral circulation returned as the skin sutures were being inserted and the recovery of consciousness and muscle power were not delayed.

Several authorities have suggested that the electrocardiographic monitoring of the heart during clinical anaesthesia should be the responsibility of the cardiologist. Several important papers have been published by cardiologists, particularly in relation to cardiac surgery (Hill, 1932; Zeigler, 1948; Campbell and Reynolds, 1952; Jaruszewski *et al.*, 1953; Campbell and Reynolds, 1954; Milstein and Brock, 1954). These reports indicate that severe cardiac disturbances often occur during anaesthesia but in most instances the observers were unable to define the precise factors which were causing the disorders of cardiac function. Writing as an anaesthetist, I should like to emphasize that the majority of cardiac disturbances, which I have described or referred to (Johnstone, 1950 *et seq.*) are due not so much to the anaesthetic agents, as to the manner in which they are used; and they are usually amenable to a physical modification of the anaesthetic technique. The accurate diagnosis of a cardiac abnormality occurring in an anaesthetized patient is based on inspection of the cardiogram combined with a detailed assessment of the clinical details of the anaesthesia—the method of ventilation, the reaction to inflation, the resistance of the air passages, the autonomic reactions to the various drugs and surgical manipulations, the fluctuations of blood pressure and pulse rate, and numerous other details with which the experienced anaesthetist is familiar.

It would appear, therefore, that the final solution to the clinical complexities of cardiovascular collapse during anaesthesia and surgery will be provided by cardiologists who are skilled anaesthetists, or by anaesthetists who are familiar with the behaviour of the human heart as depicted on the cardiogram. It is obvious that there are several different mechanisms of cardiac arrest and it is hoped that eventually we may be able clearly to define the circumstances under which they may occur and to take steps to counteract them successfully. As the number of complex drugs and techniques increases, the greater becomes the need for detailed observation of cardiovascular function during anaesthesia. It is not sufficient that this type of research should be confined to research centres for the simple reason that each anaesthetist, fortunately, encounters a relatively small proportion of the cardiovascular collapses which actually occur.

After several years experience with the electrocardiograph during clinical anaesthesia I am now quite convinced that the accurate determination of the aetiology of a cardiovascular collapse or arrest is virtually impossible in the absence of electrocardiographic records. There is a certain amount of truth in the statement that the cardiograph may record a complex when the patient is already dead. It has been my experience, however, that a tracing obtained in these circumstances shows abnormal features in at least one of the limb leads. When serial tracings are obtained before the onset of the collapse, a characteristic sequence of changes will be recognizable, from which it may be possible to determine the resuscitative measures most likely to benefit the patient. I do not wish to suggest that it is impossible to administer a safe anaesthetic without the aid of an electrocardiograph: experience always teaches us instinctively to avoid numerous pitfalls. Careful pulse palpation combined with a knowledge of pharmacology should prevent such complications as vagal arrest or ventricular tachycardia, and perhaps even the potassium intoxication syndrome. In the management of dangerously ill patients, and in the assessment of new techniques, the electrocardiograph provides information which is un-

obtainable by any other means. It is an instrument which is easily available to every anaesthetist and, quite apart from its research potential, it often provides much-needed reassurance when dealing with the critically ill patient.

SUMMARY

(1) Six different mechanisms of cardiovascular collapse during clinical anaesthesia have been described. It has been shown that each of them is associated with a characteristic sequence of electrocardiographic changes. They include collapse due to vagal overactivity, to sympathetic overactivity, to potassium intoxication, and to acute coronary insufficiency induced in three different ways.

(2) The prevention and treatment of each of these mechanisms have been described.

(3) The importance of the cardiogram in the diagnosis and treatment of cardiovascular collapse during anaesthesia has been emphasized. It is suggested that the cardiological management of the patient during anaesthesia should be the responsibility of the anaesthetist.

(4) It is claimed that pulselessness is not always an indication for immediate cardiac massage. Some of the circumstances in which the anaesthetized patient may become pulseless have been discussed.

(5) The anaesthetic management of a case of malignant carcinoid secreting " serotonin " has been described.

ACKNOWLEDGMENTS

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BOOK REVIEW

The Medical Annual. Edited by Sir Henry Tidy and R. Milnes Walker. Published by John Wright and Sons Ltd., Bristol. Price 32*s.* 6*d.*

The 404 pages of ten years ago now extend to 548.

The short section on anaesthesia and analgesia is again written by Dr. Langton Hewer. He once again emphasizes the importance of keeping an open airway, advice one would have supposed unnecessary but for the illustration on the previous page which shows in how many different ways it can be obstructed by the very means taken to ensure it. In these days of long operations and mechanical devices, the monotony of his task may render the anaesthetist temporarily oblivious of his surroundings. If this be so the "Drip alarm" figured on page 30 will no doubt provide a rude awakening and a quick recall to a lively sense of his responsibilities.

Chlorpromazine has a long paragraph to itself. Dr. Hewer refers to the well-known case of Woolley and Roe *v.* The Ministry of Health and Others. He says: "It has now been established in *law* that ampoules of analgesic solutions stored in antiseptic fluid can become contaminated even if no crack is visible." It is important for anaesthetists to remember this, but for the sake of truth they must also remember that it has not been established in *fact*. The trial decided that there was no evidence of negligence. It did not discover the cause of the damage. One witness suggested that it was the anaesthetic itself—the light nupercain—that had caused the mischief; another that it was the 1 in 40 carbolic in which the ampoules were stored. It is extremely doubtful if either of these statements will stand the test of time. What we do know is that alcohol will cause such damages as were sustained but there was no evidence at the trial to this effect.

A short paragraph on analgesic drugs by Dr. Andrew Wilson concludes this section on the subject.

Dr. Wilson later on in the *Annual* gives an account of the varying views on Nalorphine and Professor Anderson contributes an article on the use of chlorpromazine in psychiatry which also may be of interest to anaesthetists.

E. Falkner Hill

Brit. J. Anaesth. (1955), **27**, 580

EPILEPSY AND THE CONVULSIVE STATES

BY

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DEFINITION

EPILEPSY is the expression of occasional, sudden, rapid, excessive local discharge in the grey matter (Jackson, 1932). A convulsion is the involuntary tonic and clonic muscular movements to which this gives rise; the other clinical manifestations being an impairment of consciousness or other psychic function and a disturbance of the Autonomic Nervous System (Lennox, 1949a). In epilepsy, any of these clinical features or combinations of them may predominate, so the term covers a wide diversity of conditions.

HISTORY

Epilepsy was known to early Greek and Latin writers as "The Falling Sickness" and "The Sacred Disease", and it was Hippocrates who first expressed disbelief in this latter description. "It appears to me to be no wise more sacred than other diseases, but has a natural cause from which it originates like other affections" (Adams, 1843). Many famous people are said to have suffered from it, including Julius Caesar, Napoleon, Alexander the Great, Mary Queen of Scots, and Swedenborg.

CLASSIFICATION

The epilepsies are best studied in terms of the neuronal discharge which gives rise to them, and four aspects of this discharge will be considered: (1) the site of origin of the discharge; (2) the nature of the discharge (as reflected by E.E.G. readings); (3) the pathology which appears to be associated with the discharge; (4) the clinical manifestation of the discharge.

(1) *The site of origin of the discharge.*

The discharge may arise in a symmetrical and generalized manner from the central grey matter, or may originate in one specific portion of the cortex or grey matter. In the latter group, the discharge may remain localized, or spread and become generalized (Symonds, 1955).

The former group is known as generalized epilepsy (Gastaut, 1954a) (central epilepsy of Symonds, 1955), and includes two distinct types. The major seizures (*grand mal*) consist of generalized convulsions and unconsciousness. The minor seizures (*petit mal*) manifest themselves either as brief lapses of consciousness, myoclonic jerks, or loss of muscular tone, resulting in a fall. Patients describe them as blanks, jerks, and falls.

Those seizures which arise in a limited system of brain matter, often called focal, local, or Jacksonian epilepsy in the past, are now referred to as partial epilepsy (Gastaut, 1954b). They are usually associated with a demonstrable pathology, and the initial symptoms and signs in an attack are related to the site of origin of the discharge, although generalized convulsions may follow.

(2) *The nature of the discharge.*

The normal electroencephalogram, taken from a resting adult subject with his eyes closed, shows an alpha wave formation of 8–13 cycles per second. In a generalized convulsion, a quite different wave formation is seen. It consists of an increase in speed and amplitude of the wave pattern up to 30 cycles per second (Gibbs and Gibbs, 1941) and is the same whether the fit is part of a *grand mal* attack, occurs during anaesthesia, or is eclamptic in origin.

During a minor seizure of central origin, the typical wave complex consists of a rapid spike followed by a slow wave, these complexes occurring about three times per second. The myoclonic type of minor seizure more commonly shows a series of two to five rapid spikes, sometimes with an associated slow wave (Grinker *et al.*, 1938).

Cases of partial epilepsy typically show a slow wave activity related to the site of the discharge. For example, in cases of psychomotor epilepsy, who have episodes of compulsive, aggressive behaviour, the discharge can be demonstrated arising in one or both temporal lobes (Walton and Osselton, 1951a).

(3) *Associated pathology.*

Only in about 25 per cent of patients suffering from epilepsy can any related pathology be found and Lennox (1949b) divides such findings into four groups:

(a) *Congenital defects in the central nervous system*, e.g. cerebral diplasia, cerebromacular degeneration, mental defectiveness.

(b) *Acquired changes in the brain*, e.g. birth trauma, tumours, cysts, haemorrhage, arteriosclerosis, meningitis and encephalitis, abscess, general paresis, and tubercle.

(c) *General conditions and diseases.* Toxaemia of pregnancy, uraemia, malaria, infective fevers, asphyxia, oxygen intoxication, carbon monoxide poisoning, tetany, hyperventilation, hypoglycaemia, alcoholism, migraine, anaesthetic drugs, electric shock, and cerebral oedema.

(d) *Convulsant drugs.* Local anaesthetics, picrotoxin, leptazol, absinth, ergot, lead, caffeine, nicotine, camphor, and magnesium sulphate.

Most of the above-named conditions are only occasionally accompanied by fits, but their relationship to them is too frequent to be fortuitous, and it seems probable that in a small proportion of the population, who are " convulsion prone ", these lesions can act as precipitating factors.

(4) *Clinical types.*

The distinguishing features of minor seizures (*petit mal*) and partial epilepsy have already been mentioned; it remains to describe a major epileptic attack.

Motor, sensory, or psychic symptoms may precede the seizure by hours or days, and immediately before the actual fit about half the patients experience a more acute premonition of the event, the so-called aura. The nature of this aura varies as widely as do the prodromal symptoms.

The convulsion may begin with a loud cry, and, as consciousness is lost, the patient falls to the floor in a state of tonic muscular spasm, lasting about half a minute and accompanied by increasing cyanosis. This stage is followed by a series of increasingly severe tonic spasms lasting about one minute and usually accompanied by copious salivation, and loss of sphincter control. As the paroxysms abate, the patient falls into a profound sleep, on recovering from which he may perform acts of which he has no final memory. The social disadvantages of this postepileptic automatism may be serious.

Status epilepticus represents the disorder at its maximum, the sleep following one fit being interrupted by the next attack. A case is reported of a thirteen-year-old girl who recovered perfectly after having 3,231 major fits in 17 days (McDougall, 1919).

AETIOLOGY

Normal functioning of the human brain depends on its ability to limit afferent impulses to the appropriate neuronal channels, in circumstances where spread of the discharge into a host of other channels is theoretically possible. Failure to limit this neuronal release is the essential defect in epilepsy. The liability to such failure differs widely in a random group of patients and is reflected in the variable dosage of convulsant drugs required to produce fits in such a group.

Cure *et al.* (1948) demonstrated this variation using leptazol and showed that the minimum dosage in terms of body weight was regularly less in epileptic patients than in normal controls.

In the experimental animal, the main methods used to produce convulsions are electrical stimulation, convulsant drugs, and the production of epileptogenic lesions by chemicals and freezing.

The following metabolic changes have been shown to increase the liability of some patients to fits: fall in blood oxygen, abnormally high blood oxygen, alkalosis, decrease in blood calcium concentration, increase in blood chloride concentration, increase in tissue permeability, and fall in blood sugar. The reverse conditions diminish the tendency of these same patients to fits.

The occurrence of convulsions during anaesthesia has been related to: lack or excess of morphia, oxygen and carbon dioxide, impure agents, pyrexia, excessive dosage of atropine, calcium deficiency, surgical stimulation, sepsis, disturbed renal function and a specific convulsant organism (Kemp, 1944).

It seems that in the presence of one or more of these predisposing factors, a sufficiently strong stimulus may evoke a convulsion and that both the initial factor and the final stimulus may vary in different cases (Pask, 1942).

Kemp (1944) postulates that the essential mechanism is hypoxia of the cerebral tissue, thus correlating many of the predisposing factors. Oxygen requirements are raised by pyrexia and atropine, and oxygen dissociation decreased by alkalosis. This alkalosis is caused by hyperventilation which, in turn, may be due to light ether anaesthesia, pyrexia and surgical stimulation.

Brenner and Merritt (1942) suggest that a disturbance of acetylcholine metabolism may be concerned in the aetiology or mechanism of convulsions. They showed its convulsant properties when applied locally to the cortex of cats, an effect potentiated by neostigmine methyl sulphate. Fiamberti (1937) has used intracisternal acetylcholine to produce convulsions in the treatment of *dementia praecox*. Certainly, it is the only chemical normally present in the cortex which has been shown to have this effect.

During electroencephalographic examination of patients, certain methods are used to precipitate epileptic-like electrical changes. These changes persist for any length of time only in known epileptics and in a proportion of apparently normal patients who are presumably "convulsion prone". The main methods employed to induce these changes are: over-hydration, drug-induced sleep, intravenous leptazol, and audio- and photic-stimulation.

This predisposition of some patients to convulsions, even though they are not known epileptics, is borne out by the work of Williams and Sweet (1944). They followed up 42 patients who had had convulsions during anaesthesia, and out of 22 of them on whom e.e.g.s were performed 73 per cent showed abnormalities similar to those seen in idiopathic epilepsy, as opposed to 12 per cent in a normal control group. In a further series, 75 per cent of idiopathic epileptic cases showed similar changes.

Rosenbaum and Maltby (1943) studied 20 cases who had had toxaemia of pregnancy and 20 further patients in whom the condition had progressed to convulsions. When examined, 65 per cent of the latter group had abnormal e.e.g. readings, and 60 per cent a family history of fits. Of the "toxaemia only" series, 10 per cent showed abnormal e.e.g.s and 10 per cent gave a family history of fits.

It can be argued, that these e.e.g. changes have, in fact, been caused by the convulsions, and were not present before them, but such changes are seen in up to 25 per cent of people who have never convulsed (Williams, 1941) and are absent in 25 per cent of those who have (Walton and Osselton, 1951b).

In terms of neuronal stability, the population falls into three groups: the large majority who will convulse only under markedly abnormal conditions; the known epileptics whose fits occur where no obvious or precipitating factors are present; and a third group, intermediate between the two, and not known epileptics, who will convulse if presented with one or more of the predisposing factors previously listed and then with an adequate stimulus. The patients who convulsed under anaesthesia and during pregnancy, referred to in the preceding studies, would presumably be of this last group (Williams and Sweet, 1944; Rosenbaum and Maltby, 1943).

TREATMENT

Where possible, this is directed against the associated pathology, the excision of localized lesions being sometimes possible. Recently, cases of psychomotor epilepsy have been successfully treated by excision of one or both temporal lobes (Penfield and Flanigin, 1950).

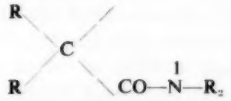
Treatment of idiopathic epilepsy is devoted to the suppression of attacks, the treatment of the fits when they occur, and the sensible but not excessive regulation of the patient's life to his condition.

Suppression of attacks.

Major epileptic seizures can sometimes be prevented and almost always diminished in frequency and severity by drug therapy. Derivatives of three main groups are used; those of barbituric acid, hydantoin, and acyl urea. Examples of each of these groups are: phenyl ethyl malonyl urea (phenobarbitone Luminal, Gardenal); sodium diphenyl hydantoinate (Dilantin sodium, Solantyl, phenytoin sodium); and phenacetyl urea (phenurone, Epielase).

Petit mal attacks respond better to derivatives of oxazolidine 2–4 dione, the main one being trimethyloxazolidone dione (epidione, tridione).

The anticonvulsive action of these drugs depends on the grouping:



Therapy must be continued for at least three years after the last fit has taken place, and toxic manifestations are an indication to change the drug and not to stop therapy. Recently, a drug of low toxicity of the dione group, primidone (Mysoline), has been introduced and found of value in both major seizures and *petit mal* (Handley and Stewart, 1952; Smith and McNaughton, 1953).

The seizure threshold can be further elevated by improving the general health, a ketogenic diet and low water intake, though these last two methods may demand considerable fortitude from the patient.

Care during a convulsion consists of preventing injury, especially tongue biting, and clearing the airway.

Status epilepticus is treated by the intravenous injection of phenobarbitone (5 grains (300 mg) for an adult) and tridione (15 grains (900 mg)). Other methods of treatment are the use of magnesium sulphate, bromides, and, as a last resort, rectal bromethol (80 mg/kg). The withdrawal of cerebrospinal fluid sometimes ends an attack, but lumbar puncture in these cases is technically difficult.

The factors predisposing to convulsions during anaesthesia, already listed, should be avoided as far as possible, but if anaesthesia has to be undertaken in their presence, barbiturate premedication, a small atropine dosage, keeping the patient cool and adequately oxygenated through a free airway, will render fits less likely.

When such convulsions occur, the administration of anaesthetic agents should be stopped, intubation performed if possible, and the lungs forcibly inflated with oxygen. An intravenous injection of a 2½ per cent solution of thiopentone sodium is then given slowly until muscle movements cease. Even when allowance is made for the slowing of the circulation time which accompanies the fit, apnoea from the thiopentone can easily result and the patient must then at once be inflated with oxygen. The muscle paroxysms can alternatively be controlled by giving a short-acting relaxant such as suxamethonium chloride, which has the merit of allowing easy intubation and inflation, and avoids further circulatory depression. However, during the convulsions, considerable assistance is required to hold a limb steady enough for intravenous injection of any sort.

Most cases of toxaemia of pregnancy do not proceed to convulsions if placed on a strict régime of bed rest and reduced fluid intake. But if fits develop, three avenues of treatment are available: heavy morphinization, rectal bromethol or paraldehyde, and continuous spinal or epidural anaesthesia, the effectiveness of the latter procedure being related to its hypotensive effect.

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QUESTION AND ANSWER

SOME THERAPEUTIC ASPECTS OF ANAESTHESIA

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QUESTION

How may the Anaesthetist help his colleagues in the treatment of their patients?

ANSWER

He can give his colleagues the benefit of his advice based on experience of certain aspects of disease and on his special way of dealing with these problems. Examples are the maintenance of a free airway, the proper interchange of gases during respiration, and the use of sedation and analgesic drugs. He can also employ special anaesthetic and analgesic techniques to ease pain and restore function. He can, in addition, give valuable assistance to his surgical colleagues in the Anaesthetic Out-patient Department.

QUESTION

How may an Anaesthetist help with the treatment of surgical patients pre- and postoperatively?

ANSWER

An Anaesthetist can readily employ simple therapeutic measures together with common sense in the Anaesthetic Out-Patient Clinic. There he can cure several important but simple conditions, and he can help other patients by detecting abnormalities which are capable of amelioration. He can by the prescription of a low calorie diet and by encouragement of the patient supervise weight reduction to the extent of two or three stone if necessary. He can cure smoker's cough by advising that cigarettes should be temporarily given up, and can relieve simple anaemia following haemoglobin estimation, by the administration of iron by mouth or intramuscularly. He can see that dental sepsis is eradicated and that faulty methods of breathing are checked. Sometimes he may even be able to cure or at any rate lessen the anxiety that some patients feel about the whole question of operation and anaesthetic.

Postoperatively the Anaesthetist should supervise and, if necessary, help in the diagnosis and treatment of such chest complications as may arise. His knowledge of the pharmacology of analgesic and sedative drugs can be put to fruitful use after operation, while he may be able to benefit the patient by taking part in the treatment of the simple complications which arise after surgical operations and anaesthesia.

QUESTION

What are the results of sympathetic dysfunction and how may they be assessed?

ANSWER

Sympathetic dysfunction can cause symptoms due to vasospasm, the production of pain, and visceral dysfunction. Thus, therapy is directed to vasodilatation, relief of pain and restoration of function.

There are several tests designed to give information about the vasomotor state of a limb, including raising the body temperature, reflex vasodilatation arising in an extremity when heat is applied to the other extremities (the so-called limb immersion method), reflex vasodilatation following temporary occlusion of the blood supply, known as reactive hyperaemia and seen in the flushing of a limb on the release of a tourniquet. This is due to dilatation of small skin vessels and is independent of the nervous system.

Lastly, and most important for our purpose, is vasomotor nerve block, and this may be achieved at any of three levels. (*a*) The peripheral nerve may be blocked, leading to paralysis of its accompanying vasoconstrictor fibres, e.g. the ulnar nerve causing vasodilatation of the little finger, or the posterior tibial nerve. (*b*) The sympathetic ganglia may be blocked by paravertebral injection, e.g. the stellate or second and

third lumbar ganglia. (*c*) The nerves may be blocked in the extradural space by either the thoracic, lumbar or sacral routes. (*d*) Finally, block may be applied inside the theca. The last two are examples of a preganglionic block and must extend, when dealing with the lower extremity, up to the tenth thoracic segment so as to paralyse all preganglionic vasoconstrictor fibres going to the limb. In addition to their use in therapy, sympathetic blocks can also influence the surgeon's decision as to the desirability or otherwise of operating in various states of sympathetic abnormality in the extremities.

QUESTION

What are the indications for sympathetic block?

ANSWER

Painful limbs due to vascular disease.

(1) Raynaud's phenomena. A series of changes described in 1862 by Maurice Raynaud as " local asphyxia and symmetrical gangrene of the extremities ". It has been defined as intermittent pallor or cyanosis of the extremities, precipitated by exposure to cold, without clinical evidence of blockage of the large peripheral vessels and with nutritional lesions, if present at all, limited to the skin. It is seen in females much oftener than males, and may be due in part to some abnormality in the somatic nerve supply to the digits (Johnson, 1941). Sir Thomas Lewis held that the primary cause was the result of a local fault in walls of the digital arteries. The results of sympathetic block are often fairly good, although even ablation of all vasoconstrictor impulses to the limb concerned does not always permanently cure the condition.

(2) Vasospasm associated with lesions of the spinal cord such as poliomyelitis and some cases of pyramidal disease.

(3) Arteriosclerosis and thrombo-angiitis obliterans, which may cause either intermittent claudication or peripheral gangrene associated with pain at rest. The former may occur without any evidence of nutritional disease. Conversely, gangrene may be seen in patients who have no history of claudication. According to Kunkel and Stead (1938) quoted by Richards (1946) the maximum blood flow of the foot, the flow at full vasodilatation, must be reduced by 66 per cent before symptoms of trophic disturbances are seen, whereas claudication may be present even if the blood flow to the foot is apparently normal at rest. It must be recalled, however, that active muscular movement may demand twenty or thirty times the normal resting blood supply and this may be regulated by metabolites produced in the muscles themselves, and not by vasomotor change. The value of sympathetic block is probably that it increases the total blood flow to a limb and not merely its redistribution to the cutaneous vessels at the expense of the deeper and more vital tissues.

(4) Chronic ulceration of the extremities.

(5) Embolism of major vessels.

(6) Thrombophlebitis, releasing reflex spasm of arteries and veins.

(7) Erythromelalgia, the opposite of Raynaud's phenomenon, with redness and painful digits.

Conditions due to idiopathic and post-traumatic pain.

(1) Causalgia, a condition of hyperaesthesia of parts of an extremity following injury in the region of a peripheral nerve. It was first noticed by Weir Mitchell in 1864 in soldiers wounded in the American Civil War. It is a very difficult condition to treat and the results of sympathetic block are variable. True cases get relief, psychosomatic ones do not.

(2) Amputation stump neuralgias.

(3) Südeck's atrophy of bone following fractures of bone, injury etc., with decalcification, loss of power in the limb, vasomotor disturbances and pain.

(4) Immersion foot syndrome, a condition which is seen in the extremities after they have been exposed to moist cold. The disease passes through three phases: firstly, the prehyperaemic, when the foot or hand is cold and pulseless due to vasoconstriction; next, the hyperaemic, due to vasodilatation caused by local release of products of metabolism formed by the effect of cold on the tissues; lastly, the posthyperaemic stage. Cold therapy is used in phase 2 and sympathetic block has been successfully used in phase 3.

Sympathetic block is useful after embolectomy, and has achieved good results in cases of hyperhidrosis of nervous origin.

QUESTION

Outline the anatomy of the autonomic nervous system involved in block of the thoracic and abdominal viscera and of the head and neck.

ANSWER

(1) *The heart and aorta.*

The sympathetic is the accelerator and augmentor of cardiac action, a fact described in 1863 by V. Bezold. Fibres arise in the intermediolateral horn cells of the cord in the first to the sixth thoracic segments, and as white rami enter the corresponding thoracic ganglia, from which postganglionic fibres pass directly to the heart—the thoracic cardiac nerves. Other preganglionic fibres ascend the sympathetic trunk to the three cervical ganglia from which postganglionic fibres—the upper, middle and lower cervical cardiac nerves—pass to the heart, on the right side to the sino-auricular node, and on the left to the auriculoventricular node and bundle.

Visceral afferents carrying pain from the heart and aorta accompany the thoracic and cervical cardiac nerves and enter the cord via the white rami of the upper six thoracic nerves, to have their cell stations in the corresponding posterior spinal root ganglia.

(2) *The abdominal viscera.*

Fibres conveying inhibition of motor impulses originate in the intermediolateral horn cells of the cord in the fifth thoracic to second or third lumbar segments. The white rami pass through corresponding ganglia without synapsing, fuse to form the three splanchnic nerves, enter the abdomen by piercing the crura of the diaphragm, and synapse in the coeliac ganglion, from which postganglionic neurones are distributed to the viscera via the vessels. The preganglionic fibres for the suprarenal come from the first and second lumbar roots. The coeliac plexus also receives contributions from the vagus and phrenic.

Visceral afferents from the alimentary canal travel with the splanchnic nerves, entering the cord on their way to the posterior root ganglia via the white rami from the fifth thoracic to the second lumbar nerves.

(3) *Head and neck.*

Anatomy. Preganglionic neurones arise from cells in the intermediolateral horn cells of the cord in the first and second thoracic segments, and pass as white rami to corresponding ganglia—i.e. the stellate and second thoracic—from which they ascend to the superior cervical ganglion. Postganglionic fibres come (*a*) from the stellate via the vertebral nerve, a plexus surrounding the vertebral and basilar arteries, and (*b*) from the superior cervical ganglion via the external carotid, middle meningeal, and also internal carotid and its branches to the brain and meninges. The oculopupillary fibres which dilate the pupil, pass out by the first thoracic white ramus.

QUESTION

Outline the technique of certain sympathetic blocks.

ANSWER

Paravertebral sympathetic block was first done by Läwen in 1923, alcohol being used for the first time by Swetlow in 1926.

(1) *Head and neck.*

Available methods are stellate block and the approach may be from the front, from behind, or from the side. As the first thoracic ganglion is blocked with its white ramus, the signs of the Claude Bernard–Horner syndrome are seen, provided that the patient has not recently had homatropine instilled into his pupils to aid neurological diagnosis.

Stellate ganglion block. This term embraces cervicothoracic sympathetic block—as when a local analgesic solution is injected into the region of the stellate ganglion, the middle cervical (and sometimes the superior cervical), the second and third and sometimes the fourth thoracic ganglia are blocked too (Moore, 1954).

As the upper part of the cervical sympathetic chain receives no nerves from the spinal cord directly, the whole of it becomes paralysed by successful stellate ganglion block. The block is usually done to abolish vasomotor tone in the head and neck and also in the upper limb. As the second thoracic ganglion shares in the infiltration, the nerve of Kuntz, a grey ramus from the second ganglion to the first thoracic nerve, becomes blocked so that vasodilatation in the arm and hand is complete. The technique is simple. The ganglion can be approached from many directions, but the easiest and safest route is from the front.

With the patient lying supine and the chin tilted up, a weal is raised two fingers' breadth, that is, 1¼ to 1½ inches, laterally to the jugular notch and the same distance above the clavicle. It should lie over the transverse process of the seventh cervical vertebra and at the medial border of the sternomastoid muscle. The position of the weal can be checked by the tubercle of the sixth cervical vertebra, which is usually palpable, and by the cricoid cartilage also at the level of the sixth cervical vertebra. The carotid sheath and sternomastoid are pulled laterally and a No. 1 needle is inserted directly backwards until it meets bone, which should be the transverse process of C.7, at an average depth of 1½ inches. It is now withdrawn ¼ to ½ inch to avoid injecting into the longus coli muscle and after careful aspiration for blood from the vertebral vessels and cerebrospinal fluid from the theca, a test dose of 2 ml is injected. If no untoward effects are noted a further 8 ml follows (Moore, 1954).

A successful block is shown by Horner's syndrome and by vasodilatation of the vessels of the conjunctiva, flushing of the face and neck and upper extremity, and anhidrosis. Nasal obstruction due to vascular dilatation of the nasal mucosa (Guttman's sign) is seen, and the patient may lachrymate. These signs may be delayed for half an hour, and their appearance signifies successful block of the cervical sympathetic, not necessarily of the second and third thoracic ganglia and vasomotor paralysis of the arm. Long-lasting effects by 6 per cent phenol or alcohol can be obtained.

Some of the indications for stellate ganglion block are: In the upper extremity thrombophlebitis, postoperative oedema, ischaemic paralysis, causalgia, herpes zoster, cervical rib, non-union of fractures and scleroderma. In the brain, cerebral thrombosis and embolism and spasm following angiography (Leriche, 1952); and quinine amblyopia (Glick and Mumford, 1955). In the heart, angina pectoris and myocardial infarction. In the lung, embolism. On the face Bell's palsy, herpes zoster and occlusion of the retinal artery.

(2) *Upper extremity.*

The second and third thoracic ganglia can be blocked from behind, or from the front as a stellate ganglion block. In addition ulnar nerve block will produce vasodilatation of the little finger. Brachial plexus block gives a marked degree of vasodilatation of the whole limb.

(3) *The heart and aorta.*

For angina pectoris, paravertebral block of the second to the fifth thoracic ganglia on the left side is the treatment of choice. In doing paravertebral blocks, where great accuracy is required, no more than 3 ml should be injected at one time, to minimize spreading. If alcohol is to be used there is great danger of causing intercostal neuritis. The patient should remain still for one hour after the injection of alcohol to minimize spreading. Only pain carried over visceral afferents can be permanently relieved by alcohol block. X-ray control of the point of the needle is useful and makes for greater accuracy.

Oily solutions, such as proctocaine, have a slightly longer effect than procaine. Benzyl alcohol has been used successfully and 6 per cent phenol in water is said to have selective action for sympathetic fibres. Alcohol block should be most carefully done and should be preceded by procaine block using only small amounts to prevent dilution of the alcohol, and only after the needle has been shown to be correctly placed by the results of procaine block should alcohol be injected.

(4) *Lower extremity.*

(1) The methods available are subarachnoid (preganglionic block), but if the blood pressure is allowed to get too low following this method, there may not be enough blood circulating to cause vasodilatation, even though the vessels are ready to receive it. Height must be to the tenth thoracic segment.

(2) Extradural (preganglionic block) by either the lumbar or sacral routes, which must also reach to the tenth segment.

(3) Paravertebral sympathetic block (postganglionic) of the second and third lumbar ganglia.

(4) Block of the sciatic nerve.

(5) Block of the external popliteal nerve just below the head of the fibula.

(6) Block of the posterior tibial nerve from a weal medial to the tendo achillis, opposite the base

of the malleolus, the needle being advanced anteriorly to the tibia and the track being infiltrated with 5 to 10 ml of 2 per cent procaine.

(5) *Abdomen.*

Subarachnoid injection of absolute alcohol was first brought to notice by the Italian anaesthetist Dogliotti, in 1935. It is suitable for intractable pain only if it is situated below the groin and iliac crests, i.e. in the lumbosacral distribution. The lumbar puncture should be relatively high up, either between T.11 and L.T.12 or T.12 and L.1. The patient is put in such a position that the bad side is uppermost, the head inclined downwards and the patient semiprone so that the posterior roots are uppermost. Autoclaved absolute alcohol 0.5 ml is injected and the patient kept in position for one hour to prevent spreading. Headache and slight fever may follow pain relief. The injection may have to be repeated in from a few days to a few months. Subarachnoid adhesions are not seen after this treatment but sphincter paralysis is a risk.

Interspinal segmental analgesia, following the technique of Tuohy (1941), has been used to control pain. A plastic catheter is placed in the theca and its position checked by radiography. Dilute procaine is injected and when a proper level of analgesia has been induced, small amounts of alcohol are injected.

QUESTION

What are the indications for sympathetic block in the abdomen?

ANSWER

Telford and Haxton (1948) have treated cases of Hirschprung's disease by subarachnoid block reaching to T.5, with variable results. Several weeks may elapse after the block before its full benefit is seen. Such a technique is simple and may let one know which way the wind blows. An opaque enema given before the block, with X-rays taken before and after it, will give, in addition, useful visual information. The whole procedure may have to be repeated (Northfield, 1950). This treatment is more successful in children than in adults.

Anuria, if due to cortical ischaemia, may often be treated successfully by block of the sympathetic fibres up to and including T.8, as described later in the treatment of eclampsia. Ammonium salts are said to have a selective affinity for C nerve fibres—the visceral afferents (Judovitch, Bates and Bishop, 1944).

The block may be spinal up to T.5 for intestinal lesions, or it may be extradural, paravertebral or splanchnic, using the method of Kappis (1920). Splanchnic injection of alcohol has given relief in inoperable cases of carcinoma of the pancreas. Paravertebral thoracic block of T.7 and T.8, and in addition sometimes T.6 and T.9, will ease the pain of biliary colic. Block of T.12 and L.1 ganglia will relieve renal colic, and the pain of acute pancreatitis is relieved by block of T.8, T.9 and T.10 ganglia.

To ascertain if all the sympathetic fibres of a limb have been blocked, a skin thermometer is useful, but the patient must be exposed to the air of the room before the block is started, to allow stabilization of temperature. As sudomotor and vasoconstrictor nerves travel together, block of one will accompany block of the other. Thus, if the patient's body is heated by an electric cradle until sweating occurs, denervated areas will remain dry. Sweat can be detected by careful inspection with a light coming at an angle, or by the use of the dye chinazirin, as described by Guttman (1940).

Retroperitoneal haematomata have followed paravertebral blocks and this and other blocks should not be performed in patients undergoing anticoagulant therapy. Other sequelae reported are osteomyelitis of the spine and paraplegia following inadvertent injection of alcohol into the theca. When sympathetic block is to be done by the extradural route, 0.5 per cent procaine or 0.05 per cent amethocaine can be used, as the sympathetic fibres are more easily blocked than either the sensory or motor fibres, perhaps because of their smaller size.

QUESTION

Give examples of the injection of somatic nerves for intractable pain.

ANSWER

Fifth nerve. Alcohol injection of the gasserian ganglion is a most useful palliative in patients who are not suitable for retrogasserian neurectomy and

who are suffering from tic douloureux—paroxysmal pain confined to the distribution of one or more divisions of the fifth nerve (Rollason, 1955). Sequelae which have been reported include herpes and keratitis. Branches of the fifth nerve may sometimes be usefully blocked, e.g. the inferior dental nerve if put out of action by a relatively long-acting analgesic, will make for comfort in patients who have a fracture of the lower jaw. Infra-orbital and supra-orbital neuralgia and herpes zoster can be relieved by either procaine or alcohol block, while good results can similarly be obtained by block of the supratrochlear and mental nerves. The facial nerve has been blocked for intractable spasm, while the superior laryngeal nerve can be blocked with 0.5 ml of alcohol in severe cases of painful laryngeal disease and to relieve reflex vagal pain in the external auditory meatus. These techniques are beautifully described and illustrated in Gaston Labat's book *Regional Analgesia* (1930). Traumatic torticollis can be a most painful and unsightly deformity, but it can be relieved by a block of the accessory nerve which leads to relaxation of the sternomastoid and trapezius muscles. It requires, in addition, a superficial cervical plexus block and this, together with the injection of 10 ml of solution such as 1 in 1000 amethocaine beneath the sternomastoid at its upper part at the level of the second cervical vertebra, will give good results. Painful clicking jaw has been relieved by procaine injection into the temporomandibular joint.

Limitation of movement of the shoulder joint in many cases lends itself to block of the suprascapular nerve at the suprascapular notch by the technique of Wertheim and Rovensteine (1941). The nerve rises from C.5 to C.6, enters the suprascapular fossa through the suprascapular notch on its way to the supraspinatus muscle and the shoulder joint. To block the nerve the patient should be sitting with his arms at his sides, the head and shoulders slightly flexed. With a skin pencil a line is drawn to mark the spine of the scapula, from the tip of the acromium to the medial border of the bone. After locating the inferior angle, a second line is drawn bisecting this angle and this is continued upwards to cross the first line. Lastly, the upper and outer of the four angles formed by the crossing of these two pencil lines is bisected, and at a point one finger's breadth on the new line, a weal is raised and a needle introduced downwards and medially to make contact with the bone of the supraspinatus fossa, just lateral to the notch. The needle is then introduced again more medially for 1 centimetre, until its point lies in the notch. Paraesthesia takes the form of pain at the apex of the shoulder, and after aspiration, 5 to 10 ml of suitable solution is injected. If the result is satisfactory and the case suitable, alcohol can later be injected.

The types of shoulder pain relieved by this technique include subacromial bursitis, calcified deposits about the capsule, and pain on abduction of the arm. The block must be at the suprascapular notch because there the nerve is accessible to a needle and no afferent branches leave it before it passes through the notch. The nerve is the sole pathway of somatic pain from the shoulder and acromioclavicular joints and structures surrounding them. An alternative technique for block of the suprascapular nerve has been described by Skillern (1954).

Phrenic nerve block.

Phrenic nerve block is a useful procedure in the treatment of persistent hiccups after operation or in patients in medical wards. The phrenic nerve only supplies the central part of the diaphragm, the peripheral part getting its nerve supply from the lower six or seven intercostal nerves. Block should first be unilateral and then, if necessary, bilateral block can be carried out by the injection of 20 ml of analgesic solution at a depth of $\frac{1}{2}$ inch along a line extending 2 inches laterally from a point $\frac{1}{2}$ inch above the sternoclavicular joint. A continuous technique has been described by Sarnoff (1951), who uses the method of electrophrenic respiration to locate the external motor joint of the nerve. A polythene catheter is introduced and strapped in position.

Thoracic somatic block.

Intercostal nerve block has been used for the relief of pain due to herpes zoster, postoperative abdominal pain, postoperative or post-traumatic atelectasis, fractured ribs or pain following the insertion of a drainage tube. In all these cases at least three nerves should be blocked.

Lumbar somatic block.

This has given good results in the treatment of herpes zoster and intractable neuritis of lumbar nerves. Fowler (1947) has advocated regional analgesia for the relief of lightning pains in tabes dorsalis. Such pains may occur on the dorsum of the foot, in the heel, over the tibia, at the back of the thigh or in the groin. Girdle pain can similarly be treated by the local infiltration of proctocaine or similar solution.

Leriche and his colleagues are warm advocates of the periarticular injection of procaine in cases of sprain, while painful scars and amputation stumps can be similarly dealt with. Painful flat feet have been benefited by the injection of procaine and a short walk (Hipps and Neeley, 1945). Lundy (1951) and his colleagues at the Mayo Clinic have recommended the blocking of the anterior and the posterior femoral cutaneous nerves for pain in the hip joint. These good results may be due in part to the anaesthetization of the deep fascia which is tender in this condition.

In patients complaining of hypertonic bladder Anderson *et al.* (1950) have recommended blocking the posterior divisions of the sacral nerves.

Mandl *et al.* (1951) have recently suggested that certain cases of incurable pain might be relieved by the injection into the frontal lobes of a small volume of procaine.

A novel therapeutic technique, although not an original one, is the intra-arterial injection described by Enjalbert (1948) and used by French and Portuguese surgeons to relieve pain and arterial spasm. Light pressure from a sphygmomanometer cuff should block venous return. The limb arteries and the abdominal aorta lend themselves most readily to this technique. For pain, procaine is used, and for spasm acetylcholine, especially in thrombophlebitis with oedema. Solutions used must not be hypertonic and if the injection causes vasoconstriction, papaverine can be injected or a stellate or lumbar sympathetic block may be combined with the intra-arterial injection. The aorta is injected from behind, similarly to the Kappis splanchnic block on the left side.

Intravenous procaine.

Techniques come and go. They are introduced, or as more often happens reintroduced, become fashionable and then gradually fade into semi-oblivion. Intravenous procaine is now fashionable, the present trend having been started by Lundy in 1942, although Leriche and Fontaine in 1935 used it for the relief of pain in occlusive arterial disease. Lewy, in 1937, recommended it for tinnitus aurium, but it was during the war when Gordon (1943) at the suggestion of Tovell (1942), tried it out to relieve the pain caused by the dressing and cleaning up of burns. This led McLachlin (1945) to use it for postoperative pain. Previous to this Burstein and his co-workers (1940) used the method for the control of cardiac arrhythmia. Since Gordon's paper, an immense amount of work has been published, most of it favourable to the drug. However, a recent paper by Keats *et al.* (1951) may start a contrary trend, for they report that in a series of 53 patients complaining of postoperative pain, 20 per cent got relief after intravenous injection of saline, 40 per cent after intravenous procaine, and 70 per cent after intravenous morphia. Because of its side effects, in their opinion, intravenous procaine has no place in the routine treatment of postoperative pain.

Good reports of its use, which is generally in 0.2 per cent solution, i.e. 1 g to each 500 ml of solution, are reported in a large variety of conditions, including:

(1) Lower nephron nephrosis with its associated oliguria.

(2) Painful vasomotor and trophic conditions such as intermittent claudication and frost-bite.

(3) Amblyopia following retinal vascular occlusion or massive haemorrhage.

(4) Orchitis and epididymitis.

(5) To speed up, by relaxation of veins, intravenous drips (Scurr and Organe, 1948).

(6) Pruritus.

(7) Serum sickness and other states of sensitivity, urticarias associated with blood transfusion.

(8) Treatment of keloids (Gordon, 1948).

(9) To control pain of operative wounds and so relieve atelectasis, making cough tolerable and aiding clearance of bronchi (Siddons and Landau, 1949).

(10) To relieve the pain in chest injury (Rook, 1951). Intravenous procaine allows strapping to be applied and saves the patient the unpleasantness of multiple needle pricks to perform inter-

costal block. Cardiorespiratory embarrassment is relieved and wet lung and atelectasis are less likely to occur.

(11) Relief of pain and spasm in anterior poliomyelitis (Smith *et al.*, 1948).

(12) To relieve pain and reduce intra-ocular tension in glaucoma.

Effect on heart. It raises the threshold for stimulation and prolongs conduction time in the ventricle. Its value in treating and preventing ventricular arrhythmias during operations in the thorax may be related to this raised threshold for stimulation. It has a quinidine-like action.

Contra-indications are myasthenia gravis and in patients who are digitalized. The drug may cause hypotension and twitching going on to convulsions.

Xylocaine has also been given intravenously (Gilbert *et al.*, 1951) in a similar manner to procaine. It has proved beneficial in the pain of general carcinomatosis. As an analgesic during labour it has proved to be less toxic and more efficient than procaine.

Procaine has been given orally to prevent pylorospasm (Roker and Lathja, 1950), and Swerdlow (1950) has experimented with its rectal installation instead of giving it intravenously, to relieve pain.

QUESTION

Indicate some therapeutic techniques in obstetrics.

ANSWER

Conduction analgesia has a definite place in the management of eclampsia, which is characterized by a spasm of the terminal arterioles throughout the whole body, especially in the kidneys. The condition is related to the lower nephron nephrosis described by Trueta, in which a renal cortical ischaemia results from stimulation of the renal vasomotor nerves, causing a diversion of renal blood flow from the cortex to the medulla and consequent cortical ischaemia and oliguria. Abolition of vasomotor tone of the renal arteries is a valuable method of treatment. Other conditions in which this block may be helpful include Weil's disease, crush syndrome, incompatible transfusions, etc.

Block, which should reach as high as the 8th thoracic segment (Lund, 1951), results in vasodilatation of vessels below the block, with consequent relief of hypertension, decreased venous return to the heart, decreased peripheral resistance, relief of pulmonary oedema, increased blood flow in the kidneys with increasing urinary output, denervation of suprarenal glands with consequent hypo-adrenalemia, temporary paresis of the muscles of the lower extremities and abdomen. Regional analgesia is preferable to general anaesthesia in toxaemia of pregnancy because of its benign effect on body chemistry.

Techniques include continuous spinal analgesia by the catheter method, with the initial injection of 6 to 12 ml of 0.1 per cent amethocaine in water which is hypobaric. Phenylephrine 10 mg may be added in some cases. A little thiopentone may be required for the purpose of the lumbar puncture. The blood pressure must not be allowed to fall too far for fear of making the baby hypoxic. Penicillin prevents infection. Bryce-Smith and Williams (1955) report good results following continuous lumbar extradural analgesia. Labour contractions can be judiciously maintained by a pitocin drip.

Continuous caudal analgesia is also most useful. As only the sympathetic nerve fibres need to be blocked, a relatively weak solution can be used, such as xylocaine 0.5 per cent or amethocaine 1 in 2000. Here again the anterior root of T.8 must be reached and its vasoconstrictor fibres blocked. Times up to 96 hours of continuous block are reported, and results are said to be good.

Uncontrollable cases of postpartum haemorrhage have been successfully treated by subarachnoid block, which causes contraction of the circular fibres of the uterus, and so cessation of bleeding. In such cases great care must be taken to see that the blood pressure does not fall to dangerous levels.

Asphyxia neonatorum.

This is often better treated by the anaesthetist than by the normal denizens of the labour ward. The initial extra-uterine inspiration is merely the continuation of normal intra-uterine respiratory function. Views differ as to the proper management of severely apnoeic babies, but it can be stated definitely that active resuscitation is required in all cases of white asphyxia. The trachea should

be intubated using a small laryngoscope, and a tube size 00 Magill or a catheter size 3 and 4 on a wire stylet inserted, and the respiratory tract ventilated with oxygen at a slight positive pressure. Intermittent positive pressure acts as a stimulus to breathing, although it probably does not of itself open up alveoli to any extent. It is expiration against a closed glottis, as in crying, which opens up the baby's alveoli. Oxygen is certainly absorbed from the mucosa of the bronchi as it also is from the lining of the stomach and small bowel. For babies in whom circumstances make endotracheal intubation impossible, a double tube modified from a Miller Abbott tube can easily be inserted, as recommended by Ostry (1951) and oxygen insufflated into the stomach. While carbon dioxide is theoretically contra-indicated, many experienced workers would not wish to be deprived of its judicious use. It is helpful to remember that in newborn babies, periodic respiration is not of serious significance. It is very frequent in the premature.

The new method of electrophrenic respiration must be mentioned. An electrical machine is used which stimulates rhythmic respiration when its electrodes are applied over the phrenic nerve in the neck (Sarnoff *et al.*, 1950), and Cross and Roberts (1951). As with all methods of resuscitation, a clear airway is necessary. While in adults phrenic stimulation inhibits respiratory movements, in babies this is not so. The apparatus produces a biphasic pulse of 3 milliseconds duration at a frequency of 60 per second. By means of a motor-driven potentiometer the intensity of the stimulus may be cycled from zero to maximum to zero at rates between 8 and 60 cycles per minute. The stimulus, when properly applied to the intact skin over the phrenic nerves, causes alternate contraction and relaxation of the diaphragm, as in normal respiration. This method of artificial respiration can, of course, also be applied to adults suffering from various types of respiratory paralysis, e.g., poliomyelitis, drowning, gas poisoning, narcotic poisoning.

A new method of treating asphyxia neonatorum is that described by Bloxsom (1951), who puts the baby in an oxygen air lock which subjects it to intermittent positive-negative pressure, to simulate its physical state *in utero* and to aid expulsion of debris and fluid from the air passages during the negative phase. The child is provided with moisture and warmth, while the pressure varies between plus or minus 1–3 lbs. at one-minute intervals.

In general, the well-balanced advice of Nixon and Ransom (1951) cannot be bettered in the management of respiratory deficiency in infants. They advise keeping the air passages clear, maintaining warmth, and giving oxygen, supplying mild sensory stimuli together with passive movements of the limbs. They stress the possible dangers of carelessly applied artificial respiration and the limits of analeptic drugs.

QUESTION

What are the indications for oxygen therapy?

ANSWER

This comes within the province of the anaesthetist. It is well to bear in mind that the indication for oxygen therapy is a lowered oxygen saturation of the blood, and the only sure way to determine this is by the Milliken oximeter or one of its modifications, which is attached to the patient's ear (Stephen *et al.*, 1951). The beneficial effects of oxygen are famous, in suitable cases, but there is another side of the picture which is often overlooked, and this is the adverse effect of giving oxygen. Sudden administration of high oxygen atmospheres to hypoxic patients may cause somnolence and even coma, especially if they are suffering in addition from a raised blood carbon dioxide content. The mechanism of this untoward state may be cerebral vasospasm, increased cerebrospinal fluid tension, direct depression of the cerebral cortex by oxygen, but is most probably due to carbon dioxide narcosis. It is often advisable to commence with the patient inhaling 30 per cent of oxygen with a gradually increasing amount added as may be necessary. When giving oxygen beware of the fire hazard and remember the glowing splinter of wood which burst into flame when the chemistry master plunged it into a jar of oxygen. In cases of emergency a cylinder of oxygen from the local garage will give oxygen quite pure enough for inhalation, and it will prove very much cheaper than medicinal oxygen. It contains a slightly greater amount of nitrogen than the latter.

QUESTION

What do you know about refrigeration therapy?

ANSWER

This is a very old method of treatment which has had fresh attention given to it since its renaissance in the early 1940s by Crossman and Allan and their colleagues. When the temperature of a tissue is lowered to 10°C there follows a great reduction in its metabolism, while conductivity of sensory impulses is entirely abolished at temperatures below about 25–30°C. In cases of vascular occlusion, when heparin, heat and vasodilators have proved useless, cold is indicated. Its good effects include relief of pain and shock, slowing of the process of clot extension, preservation of the vessel wall so that embolectomy may be later performed, reduction of exudation, infection, and tissue devitalization, and delayed absorption of products of tissue destruction. Badly traumatized limbs should be refrigerated until a patient is able to be conveyed to a surgeon. A leg can be chilled up as far as the knee without a tourniquet. By itself, refrigeration never cures, but it is a useful adjunct to treatment if commenced before tissue vitality has been lost.

Use has also been made of local refrigeration by ethyl chloride, and it is stated that if a spray of this drug is directed to parts of the body plagued by such rheumatic pains as myalgia, fibrositis, stiff neck, lumbago, etc., real relief is often obtained. The pain from sprained ligaments and tennis elbow may also be eased (Macdonald, 1943).

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INTRA-ARTERIAL THIOPENTONE

BY

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THE incidence of this accident has been variously estimated from 1 in 55,000 (Cohen, 1948) to 3 in 25,000 (Lundy, 1942). In 24 recorded cases, 9 developed gangrene. Of these, 6 required amputation of the forearm and the remaining 3 lost one or more digits. This amply illustrates the grave consequences of such a mishap.

ANATOMY

The brachial artery normally divides into the radial and ulnar arteries one centimetre below the elbow joint. At the elbow joint it is covered by the bicipital aponeurosis and deep fascia, which separate it from the medial cubital vein.

The ulnar artery is abnormal in 8 per cent of cases (Gray, 1954), when it arises above the elbow joint and may lie superficial to the flexor muscles in the forearm, lying commonly beneath the deep fascia or more rarely between the fascia and the skin.

The radial artery is abnormal in 12 per cent of cases (Gray, 1954), when it arises higher than usual and may run on the deep fascia instead of beneath it.

PATHOLOGY

The first response of the artery to intra-arterial thiopentone is intense spasm. This spasm by reducing the blood flow allows prolonged contact of the thiopentone (pH 10.5) with the intima. Thus the essential lesion is intimal damage permitting intra-arterial thrombosis. The extent of the thrombosis is related to the extent of retrograde spread of the thiopentone in the arterial tree. Rapid injection of large volumes and occlusion of the main artery by tourniquet will permit the high ascent of thiopentone into the main vessel of the arm, namely the brachial artery. Similarly the brachial artery is more readily involved if the injection is given into the medial aspect of the cubital fossa. Thrombosis of the brachial artery commonly results in amputation of the forearm.

The thrombosis occluding the arterial lumen may be complete within a few hours. Alternatively thrombosis may progressively encroach inwards from the intima leaving a narrow channel which in time may suddenly become occluded. This may account for the persistence of a pulse in some cases for as long as fourteen days after the incident before gangrene sets in.

CLINICAL FEATURES

Agonizing pain, described as burning or scalding, spreading down the forearm into the hand immediately follows intra-arterial injection of as little as 2 ml. of 5 per cent solution of thiopentone. This pain is the most constant feature and is rarely absent.

Onset of anaesthesia is delayed and its duration transient.

Pallor of the hand follows an initial red flush. This pallor may be associated with spasm of the vessels and so may persist on and off for days. Associated with the pallor is a lowering of skin temperature, both being an index of the impaired circulation. Occasionally cyanosis of the tips of the fingers or the nail beds is present.

The radial and ulnar pulse persist in most cases and may only be absent after a period of hours or days.

Mottled blue skin patches are commonly seen within a few hours distributed above and below the site of injection.

Oedema of the forearm occurs in about ten per cent of cases. It is possibly due to thiopentone entering the vascular muscle bed. (Fuhrman, 1951) and may be associated with flexion of the fingers.

Gangrene will develop in the ischaemic areas should the condition fail to respond to treatment.

TREATMENT

The treatment aims at immediate dilution of the thiopentone, reduction of local spasm, general vasodilation of the limb, and anticoagulant therapy.

5 ml. of 2 per cent procaine or lignocaine are injected immediately, preferably through the needle left *in situ*, into the affected artery. The most successful results have been associated with this procedure (Culbert, 1954; Rollason, 1950; Swerdlow, 1954).

Proceed with general anaesthesia to reduce sympathetic tone in the arm (Abramson, 1944). Deep anaesthesia causing fall of blood pressure and cardiac output should be avoided. It is interesting to note that this accident has not been observed in a case already anæsthetized.

Brachial plexus block should be carried out and repeated at intervals particularly if pallor due to spasm is present. This may be necessary up to fifteen days in difficult cases. Alternatively stellate ganglion block may be used. Lignocaine 1 per cent has the advantage of rapid action but cinchocaine 1/1,500 is useful for its long-lasting action.

Full heparinization is desirable but can only be given if no operation is performed. A large initial dose of 15,000 units is given intravenously (Cohen, 1948) followed by a maintenance dose either by a continuous intravenous drip or four-hourly intramuscularly by injection to prolong the clotting time to the region of fifteen to twenty minutes. It is advisable to continue the administration for several days as long as there is danger of intra-arterial thrombosis.

Should operation be imperative, it must be decided whether the benefits of reduced thrombosis in the arm following the use of heparin outweigh the risk of uncontrollable haemorrhage (Medico-Legal, 1954), even although this may be minimized by careful surgical attention to the bleeding points. It is useful to remember that 1 mg of protamine sulphate neutralizes 100 units of heparin.

Reflex heating. By heating the other limbs, reflex vasodilatation results in the affected limb which should not in itself be heated. The patient should be given hot drinks and kept as warm as is comfortable.

Drugs causing vasodilatation, such as papaverine 40 mg in 20 ml saline, or tolazoline (Priscol) 50 mg in 5 ml saline, may be given into the affected artery or the subclavian artery with great effect (Dundee, 1953; Edwards *et al.*, 1952; Woolmer, 1953). Tolazoline may be given orally 25 mg six-hourly. Morphine or preferably pethidine reduces vasoconstriction due to pain.

Direct surgical treatment of the arterial lesion has been extremely disappointing. Operations such as arteriectomy are of dubious value. Early arteriotomy with the hope of recanalization may be worth while (Van der Post, 1942), but as yet has had only slight success. Late surgery is hopeless.

Care of the affected limb. The limb is wrapped in a sterile towel and covered with cotton wool. It should neither be cooled nor heated and should be kept under observation for colour, temperature and pulse.

PREVENTION

The use of a more dilute solution of thiopentone, e.g. 2½ per cent, may reduce the severity of such an accident. It is interesting to note that of the 9 cases of gangrene, 6 were produced by a 10 per cent solution, 3 by a 5 per cent solution and none by a 2½ per cent solution as yet recorded. If veins are difficult to find, especially in shocked cases or in children, a 2½ per cent solution would seem to be the solution of choice.

The site of injection. It is preferable to avoid areas containing major arteries such as the medial aspect of the cubital fossa, as accidents are more

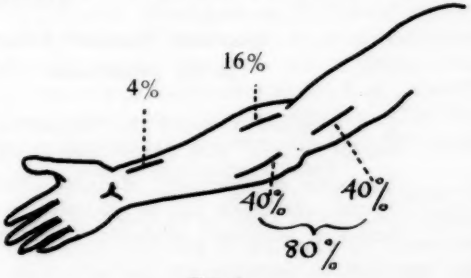

FIG. 1
Distribution of Recorded Accidents.

common and have more serious consequences in these areas (fig. 1). Even the lateral aspect of the cubital fossa and the lateral aspect above the wrist are not entirely immune (Fell, 1953). The back of the hand contains no superficial arteries and in difficult cases should be the site of choice.

Selection of the vein. The vessel should be palpated before the tourniquet is applied, since the tourniquet may prevent appreciation of any impulse in the vessel. In shocked cases pulsation may be too feeble to decide.

Method of injection. If the needle is first inserted without the syringe being attached, it may be possible to recognize bright arterial blood which may spurt if the tourniquet is correctly applied and the needle used is not too small, e.g. No. 12–14 hypo. In shocked cases hypotension and stasis invalidate this sign.

A test dose of 2 ml of 5 per cent thiopentone is given with tourniquet released, followed by a pause, and the patient is then asked if he feels any pain (Macintosh and Heyworth, 1943). In a fit adult 1 ml may be inadequate to produce this response.

CONCLUSION

This accident may suddenly face the anaesthetist at any time without warning. Constant vigilance and adherence to a technique involving routine precautions should do much to lessen its incidence.

Certainly in difficult cases such as young children and shocked patients, if thiopentone is used it would seem advisable to use a 2½ per cent solution given into the back of the hand.

Should the accident unfortunately occur, immediate treatment gives the best chance of mitigating its consequences.

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ANAESTHESIA FOR REPAIR OF THE CLEFT LIP AND PALATE

BY

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IN this country, one child in every 1,200 is born with a cleft lip or palate (Roberts, 1950). Possible causes are the inheritance of a Mendelian recessive character (Browne and Browne, 1955) or a nutritional deficiency in the mother during the first ten weeks of pregnancy. In 20 per cent of cases there are other abnormalities. Some of these, such as congenital cardiac lesions (Holdsworth, 1951) or Klippel-Fiel syndrome where a rigid cervical spine prevents flexion of the head and neck, may present additional anaesthetic problems.

SPECIAL FEATURES

The cleft lip and palate cause mouth breathing, deficient sucking and later impaired speech. The mouth breathing predisposes to chronic upper respiratory infection which may be exacerbated by periodic bouts of bronchitis. Not only, therefore, are these patients difficult to induce and intubate but they are also prone to postoperative respiratory complications. Deficient sucking may lead to malnutrition with associated anaemia. Thus these children tend to be in poor general health. This can be improved sufficiently by the age of 3–6 months to make repair of the lip feasible. The cleft palate is repaired by 18 months before speech commences.

The operative mortality has fallen from 3.8 per cent (Veau, 1938) to 0.2 per cent (Davies and Danks, 1953). This is largely due to improvements in anaesthetic techniques, particularly the routine use of intubation. However, hyperthermia which accounted for 8 of the 13 deaths in Veau's 500 cases was also the cause of the one death in Davies and Danks's 500 cases.

GENERAL FEATURES

The child has relatively a smaller blood volume than an adult, being 50 ml/lb body weight Sundermann and Bonner, 1949). The circulation time is shorter so that a smaller volume of blood is doing more work. Any loss of blood is quickly felt and should it exceeed 50 ml, it must be replaced (Blackman, 1950).

The child also has a smaller effective lung volume (Rees, 1950) than an adult but a higher metabolic rate. With such little respiratory reserve, the child tolerates badly any impairment of its airway.

The deadspace of the airway must be minimal (Stephen, 1950) as the tidal volume at 3 months is only 25 ml (Brock, 1932). The resistance of the airway must be minimal to obviate hypoxia, hypercarbia and exhaustion of the child's respiratory muscles. Obstruction of the airway must be prevented, whether it be due to surgical interference, gag pressure, debris in the air passages, the tongue falling back, or laryngeal spasm.

Intubation is generally held to be the best solution to these problems despite its imperfections (Stephen and Slater, 1949; Woodfield-Davies, 1954).

ADVANTAGES AND DISADVANTAGES OF INTUBATION

Intubation provides the child with a reliable airway, ensuring quiet and efficient respiration at all times. Deadspace can be reduced to 9 ml (Stephen, 1952) and most causes of obstruction are eliminated. Thus the risk of hypoxia and respiratory acidosis is minimized. Light, smooth, even anaesthesia is easily maintained. The surgeon has free access to the mouth and a pharyngeal pack prevents inhalation of debris.

The tube itself, however, may reduce the tracheal lumen by as much as one-third (Jefferson, 1950) but this is acceptable as it is more than offset by the reduction of deadspace and freedom from obstruction. More serious is the risk

of postoperative tracheitis and laryngeal oedema occurring in 1–3 per cent of cases (Stephen and Slater, 1949; Smith, 1953). The latter complications are largely avoidable by careful technique (Smith, 1953).

Everything considered, the advantages outweigh the disadvantages (Eckenhoff, 1951).

PRE-OPERATIVE CONSIDERATIONS

These children are admitted for 3–4 days prior to operation in order to assess their general condition, to ensure that they are not incubating an infectious or other disease, and to allow for the examination of nasal and throat swabs. Before operation can be undertaken, the child should weigh at least 10 lb and be gaining weight.

An undernourished child is placed on supervised feeding and its diet supplemented as necessary. The haemoglobin must be normal for its age, i.e. 70–80 per cent. Any anaemia is treated with oral iron and if necessary a blood transfusion is given pre-operatively. Operation is postponed in the presence of sepsis particularly of the skin, ear, nose, throat and chest, or if throat swabs taken on 3 successive days reveal haemolytic streptococci, Vincent's or diphtheria organisms. With the advent of antibiotics, surgery is no longer restricted to the summer season.

Prior to operation, the child is placed on prophylactic penicillin and given half-quantity feed diluted half-and-half with 10 per cent glucose, 4 hours before operation (Woodfield-Davies, 1954; Jefferson, 1950).

Premedication.

Atropine alone is strongly advocated by most authorities in doses of 1/200–1/100 grain according to the child's age (Woodfield-Davies, 1954; Rees, 1950; Daplyn, 1946; Aserman, 1947; Jefferson, 1950; Davies and Danks, 1953). It has been said to be the cause of the hyperthermia sometimes seen in these children (Blackman, 1950; Westhead, 1951; Woodfield-Davies, 1954), but in small doses this does not appear to be the case (Bigler and McQuiston, 1951).

Depressant drugs may be combined with atropine in children over the age of 2 years. Barbiturates may be given by mouth according to age but are not always easy to administer. Furthermore, vomiting and slow absorption make their effect unpredictable. Given rectally, on a weight basis, they are perhaps more reliable (Deming, 1952), but may be expelled (Leigh and Belton, 1950). In general, therefore, it would seem that the barbiturates are inferior to the opiates because of their variable action and because they lack analgesic properties.

Opiates given on the basis of weight (Westhead, 1951) or weight and nervous temperament (Anderson, 1952) have been recommended particularly if combined with scopolamine (Stephen and Slater, 1949; Leech, 1935; Leigh and Kester, 1948). However, as already stated, the weight of opinion undoubtedly favours the use of atropine alone, especially in the younger age groups.

INDUCTION

Many agents have been used for induction, in particular nitrous-oxide–oxygen–ether sequence, vinesthene and ethyl chloride. Using the semi-closed method, induction is made easier and smoother (Deming, 1952), and the oxygen tension of the inhaled gases is under control. The introduction of ether may be facilitated by the use of small amounts of vinesthene. Cyclopropane can also be used for the same purpose but has a smaller margin of safety.

Using the open method, oxygen should be run under the mask to prevent hypoxia (Stephen, 1952; Faulconer and Leterell, 1949). Ethyl chloride is used by some (Segal, 1947) but others prefer vinesthene, considering it to be safer (Stephen and Slater, 1949; Leigh and Kester, 1948).

In general, owing to ease and control of administration, the nitrous-oxide–oxygen–ether sequence using the semi-closed method is to be preferred.

Intubation.

Anaesthesia is deepened until the jaw is fully relaxed and the laryngeal reflexes are subdued so that smooth unhurried atraumatic intubation may be performed. If the level of anaesthesia be too light, laryngeal spasm, bucking, reflex apnoea, arrhythmias and even persistent bronchospasm may ensue (Deming, 1952; Smith, 1953, 1954).

The child's larynx differs from that of the adult in being more cephalad (Negus, 1930). The epiglottis is longer, stiffer and more U-shaped, making an angle of 45 degrees with the larynx. The

larynx itself also differs in that the cricoid ring is the narrowest diameter and here the larynx is entirely surrounded by cartilage. Thus while the cords are distensible, the cricoid is not (Eckenhoff, 1951). The cricoid then is the most vulnerable area and any trauma here readily produces laryngeal oedema. Therefore the size of the tube is carefully chosen; too large a tube predisposing to laryngeal oedema, too small a tube unnecessarily restricting the airway (Smith, 1953). Only when the larynx is actually visualized can the correct tube be chosen from a previously prepared selection. It is essential that no force be used in passing the tube and should the tube be accepted by the cords but not by the cricoid, it should be removed (Eckenhoff, 1951) lest irritation from the respiratory movements produce laryngeal oedema (Smith, 1953). Rarely the tube may enter a bronchus (Leigh and Kester, 1948), and this is indicated by jerky diaphragmatic movements and laboured breathing (Ayre, 1937).

Various tubes are in common use. The ordinary endotracheal tube is used (Davies and Danks, 1953) but is liable to kinking and obstruction particularly due to pressure from the gag, and so needs great care in its use. To avoid this problem, many prefer using reinforced tubes such as the Denis Browne with double walls (Aserman, 1947; Westhead, 1951), the Magill armoured tube (Magill, 1947), or one of reinforced latex. The Humby and Hawksley gag and tube has also been used (1943).

Nasal intubation is rarely used as the tube distorts the lip and nostril. It also interferes with the repair of the palate (Woodfield-Davies, 1954; Humby and Hawksley, 1943; Holdsworth, 1951; Smith, 1954). For these reasons the oral tube is generally preferred.

Introduction of the oral tube may be hindered by an anteriorly displaced premaxilla obstructing the field of vision and the passage of the tube. This is a consequence of a normal laryngoscope blade sinking deeply into the wide cleft. This difficulty may be overcome by packing the cleft with gauze (Leigh and Belton, 1950), bridging it with a spatula (Aserman, 1947), or by the use of a special laryngoscope (Smith, 1953; Woodfield-Davies, 1954; Davison, 1951). Occasionally the tube may impinge on the anterior inferior attachment of the cords but this can be overcome by flexion of the neck (Eckenhoff, 1951).

MAINTENANCE

Ether is generally regarded as the safest agent for maintenance (Woodfield-Davies, 1954; Stephen and Slater, 1949), using 3–4 l./min of oxygen or nitrous oxide and oxygen as vehicle. Vinesthene has been used by Daplyn (1946). Chloroform, used by Veau (1931), is no longer acceptable.

The apparatus used for maintenance must possess minimal resistance (Macintosh and Mushin, 1946) and permit no rebreathing. For these reasons the Ayre's T-piece principle is commonly employed, either as originally described by Ayre (1937) or its modification as described by Scott (1950).

Alternatively a lightly loaded non-return valve may be used (Stephen and Slater, 1948, 1949; Stephen, 1950, 1952; and Fink, 1954). The semi-closed method is not suitable as it may permit undue rebreathing to occur. Light anaesthesia is maintained just sufficient to prevent gagging and limb movements until dissection is completed and the stitching commences when the ether is discontinued to allow the early return of the pharyngeal reflexes (Ennis and Sherman, 1951).

During the operation, which should not exceed one hour's duration, a careful watch is kept on the colour of the blood. The pulse and respiratory movements are also observed. This may be conveniently done by strapping a stethoscope in the suprasternal notch where both are clearly heard and their character readily assessed.

Prior to extubation, 100 per cent oxygen is administered to mitigate the consequences of laryngeal spasm should it occur. Careful pharyngeal toilet is now carried out. The child, who by this time should be awake and crying (Woodfield-Davies, 1954), is then returned to the ward in a semiprone position.

Postoperatively the baby should be prevented from excessive crying to avoid rupture of the suture line. This is best achieved by lifting and nursing the child and feeding whenever the child is sufficiently conscious to accept it.

POSTOPERATIVE COMPLICATIONS

Respiratory obstruction may be an early complication as the air passages have been reduced by surgery and oedema. For this reason, at the end of the operation, many surgeons insert a stitch through the tongue so that it can be pulled forward to clear the airway.

Tracheitis or oedema of the larynx may occur within a few hours of operation, particularly if intubation has been traumatic (Dwyer *et al.*, 1949). It has been shown that 1 mm of oedema uniformly round the larynx at this age reduces the tracheal lumen by 49 per cent (Eckenhoff, 1951; Fink, 1954). Laryngeal oedema has a high mortality rate. Clinically the child becomes restless, pale but not necessarily cyanosed, it has a croupy cough and later increasing stridor. Palliative treatment is the administration of 60–70 per cent oxygen in an oxygen tent with 70–75 per cent humidity (Smith, 1953). Antibiotics are given and an aerosol may be used to liquefy the secretions.

Active treatment is by bronchoscopic aspiration of secretions and if necessary tracheotomy (Eckenhoff, 1951; Hollinger and Johnson, 1950).

Bronchitis and bronchopneumonia occasionally follow operation and are appropriately treated.

Hyperthemia—which may result from too hot a theatre, heavy draping of the child during operation, excessive atropine or upset of the heat regulating centres by the anaesthetic—is treated by cooling, using simple sponging, cold water mattress (Bigler and McQuiston, 1951), cold water enemata (Holdsworth, 1951), or intragastric cooling (Khalil, 1954).

CONCLUSIONS

The safety of the patient is the prime consideration since the operation is one of election. Careful pre-operative attention is necessary before the child is accepted for surgery. Improved anaesthetic techniques adapted to meet the needs of these children, particularly in the use of routine atraumatic intubation and the use of antibiotics, have all contributed to reduce the mortality rate. Another factor has been the concentration of these cases in units specializing in this work (Woodfield-Davies, 1954).

SUMMARY

A general review of the anaesthetic problems encountered in cleft lip and palate surgery has been presented. In particular the physiological considerations of this age group, the necessity for intubation, and the need to use non-rebreathing techniques have been discussed.

Methods of premedication, induction, and maintenance are considered.

Postoperative complications and their treatment are outlined.

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BOOK REVIEW

Atlas de Chirurgie Thyroidienne. By J. Francillon and G. Gabrielle. Published by Les Annales de Chirurgie, France. Pp. 179.

This book can be recommended to all interested in surgery of the thyroid. Although it is stated in the preface that it is written primarily for the inexperienced thyroid surgeon it may well be read with much profit even by the most expert.

The title "Atlas" is too modest. It is in fact an extensively illustrated monograph and both the text and illustrations are of a very high order. It is in no sense merely a collection of the classical techniques. A separate chapter is devoted to each main step of the operation; anatomical details are described and illustrated and at each point the various classical techniques which are applicable are discussed in detail with their advantages and disadvantages. Special attention is devoted to consideration of the various pitfalls that may confront the thyroid surgeon and how to avoid them.

Chapters are also devoted to the recurrent laryngeal nerve and the parathyroid glands. These contain much valuable detail and will well repay reading by the British surgeon whether he practises exposure of these important structures in his routine operation or not.

In so far as the Anaesthetist is concerned, if he believes, as I think he should, that it is of advantage in the administration of the anaesthetic to have a precise knowledge of the technical details of the operation, this book will provide him with that information. The examination candidate too may turn to these pages for much valuable information.

Philip Hawe

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ANNOTATION

POSTGRADUATE EDUCATION IN ANAESTHESIA

POSTGRADUATE education should seek to inculcate the wide knowledge and breadth of vision essential to a balanced and critical outlook. This is, perhaps, even more desirable in the education of those who are to practise a comparatively restricted field of medicine. The administration of anaesthetics by the relatively few agents and methods available in the past was one of the most restricted of those fields. Indeed, it was generally recognized that the interests of the patient would be better served by an experienced nurse than by a professor of pharmacology. If full advantage is to be taken of the striking advances of the last twenty years, the expert technician no longer meets the case—but neither does the professor of pharmacology. With a wide knowledge of theory must be combined a high degree of technical skill.

Practical experience was often acquired without instruction or supervision: in many hospitals it was, in fact, necessary to surpass the standard accepted by the visiting staff in order to approach one that would be regarded as commonplace today. Self-instruction is no longer justifiable, as it involves risk of the sacrifice of patients in covering ground which has already been fully explored by the pioneers: nor is it any longer necessary when most hospitals have skilled and experienced men available to provide the instruction. The extent of supervision must vary greatly, as it is a direct responsibility of the instructor; but, in many inadequately staffed hospitals, it is often much less than is desirable. Yet many anaesthetists, quite properly, practise only a few techniques which they have tried and found satisfactory. The anaesthetist in training, if his education is not to be unduly limited, must not be restricted to the techniques favoured by his senior colleagues. Ideally, his experience should be gained in a number of hospitals, including the special units which, increasingly, are being separated from the general hospitals.

Theoretical knowledge is most rapidly and agreeably acquired by informal discussion; but, as such discussions must be heavily weighted by personal opinions, and as they can cover only a part of the field, they are no substitute for systematic reading and lectures. Twenty years ago it was possible, in the time spared in six months of a busy resident appointment, to keep pace with the current medical literature, to read all the English language textbooks on anaesthesia and related subjects, some of them a number of times, and to pursue into original papers some interesting points which had been imperfectly understood by the authors of some of those textbooks. This is now manifestly impossible: but the books must be read. To my mind there is little value in lectures which repeat or summarize material that is already easily available. The lectures at the Faculty of Anaesthetists are, accordingly, planned to cover, largely, subjects which appear to require further elaboration.

To keep abreast of current opinion on anaesthetics and allied subjects is, alone, something of a *tour de force*. But much of this opinion, dogmatically expressed, derives from wrong conclusions formed by faulty reasoning from false premises and from uncritical interpretation of valueless data! It is here that the student most needs assistance: by drawing his attention to important developments in fields outside his immediate range; and by guiding him past the sirens of extravagant claim and counterclaim until his knowledge is sufficient to enable him to form his own critical judgment. And it is here that the Educational Supplement of this Journal has already given him valuable service with a wide range of authoritative and critical reviews.

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ADRENALINE AND NORADRENALINE

BY

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HISTORY

THE adrenal glands were described in 1563 by the great anatomist of the Renaissance, Bartholomaeus Eustachius. For nearly three centuries their function remained obscure, a fact well illustrated by the offer of a prize from the Bordeaux " Académie des Sciences " in 1716 for the best thesis on the subject " Quel est l'usage des glandes surrénales?" No contribution was found worthy. During the earlier part of the nineteenth century, however, anatomical studies revealed the glandular nature of the adrenal cells, and the relationship between the glands and the nervous system was noted. Modern knowledge of adrenal physiology rests on the foundation laid by Thomas Addison in 1855, when he described eleven cases of the disease which bears his name.

Detailed research on the adrenal medulla began in 1895, when Oliver and Schaefer published their classic paper describing the pressor effects produced by the intravenous injection of adrenal extracts. Their findings were confirmed independently and almost simultaneously in Poland (Szymonowicz and Cybulski, 1895), and the pressor material was shown to be present in adrenal venous blood. In 1901, an active principle was isolated by Takamine, who named it " adrenalin ", and by Aldrich. Adrenaline was synthesized by Stolz in 1904 and also by Dakin in 1905; in the latter year, Starling (1905) introduced the word " hormone " (ὁρμάω—I excite). Adrenaline was the first hormone to be synthesized.

It soon became apparent that the effect on an organ of injected adrenal extracts closely resembled the effect on that organ of sympathetic stimulation (Lewandowsky, 1899; Langley, 1901). From this observation developed the theory of neurohumoral transmission, first suggested by Elliott in 1904.

For nearly fifty years it was to be the generally accepted view that sympathetic nerves produced their characteristic action by liberating adrenaline, but as early as 1910 Barger and Dale had doubted this. " The conception of sympathetic nerve impulses as acting by liberation of adrenine seems to us unsatisfactory . . . it involves the assumption of a stricter parallelism between the two actions than actually exists." They emphasized the more prominent inhibitor effects of adrenaline, and continued: " The action of some of the other bases, particularly of the amino . . . bases of the catechol group, corresponds more closely with that of sympathetic nerves than does that of adrenine." One of the amino bases studied by Barger and Dale was noradrenaline, which had been synthesized previously by Stolz (1904), who had noted its powerful pressor action.

In 1921 Loewi showed that sympathetic nerve stimulation liberated an adrenaline-like substance into frog's heart, but in the same year Cannon and Uridil (1921) observed that the remote effects produced by (splanchnic) hepatic nerve stimulation in the cat were not identical to the effects of adrenaline. This led to the evolution of the " sympathin " theory, suggested by Cannon and Rosenblueth (1933). They postulated the existence of sympathin I (inhibitor) and sympathin E (excitor), formed in each case by a primary mediator, adrenaline, with constituents in the reacting cells.

In 1934 Bacq modified the theory by suggesting that while the inhibitor substance was adrenaline, the excitor agent was non-methylated adrenaline, i.e. noradrenaline. This view, that noradrenaline played an important role in sympathetic nerve transmission, was shared by others (Stehle and Ellsworth, 1937; Melville, 1937; Greer *et al.*, 1937), but in 1939 support for the original " sympathin " theory came from the finding by Cannon and Lissák of a sympathomimetic substance, which they considered to be adrenaline, in organ and nerve extracts. Subsequent studies by von Euler (1946c) questioned Cannon and Lissák's interpretation of their own experimental findings.

In 1944 Holtz (1947) and his colleagues

demonstrated the presence in urine of a substance behaving like noradrenaline. In several important papers von Euler (1946a, b, c) described the finding of an agent with the properties of noradrenaline in mammalian heart, sympathetic nerves, and various organs. Gaddum and Goodwin (1947) also showed that a substance resembling noradrenaline was released by stimulating the sympathetic nerves to the liver.

Proof then followed of the existence of noradrenaline in the adrenal medulla (Holtz and Schumann, 1948; Euler and Hamberg, 1949; Goldenberg *et al.*, 1949) and in adrenal medullary tumours (Holton, 1949); also, it was shown to be present in adrenal venous blood (Bulbring and Burn, 1949). In 1949, the chemical isolation of noradrenaline from the adrenal gland was accomplished (Bergstrom *et al.*, 1950; Tullar, 1949).

OCCURRENCE AND DISTRIBUTION OF ADRENALINE AND NORADRENALINE

Careful biological analysis of extracts of sympathetic nerves, and of organs supplied by their fibres, revealed in 1946 that the sympathetic substance had the characteristic properties of noradrenaline (Euler, 1946a, b, c).

The noradrenaline content of different organs shows considerable variation, but is related to the richness of the sympathetic supply. Lung and striated muscle, for example, contain only small amounts, while the spleen of animals is relatively rich in noradrenaline. The placenta, which is nerve-free, contains no catechol amines (Euler, 1951). It has been suggested that adrenaline and noradrenaline are actively formed in arteries (Jiménez-Diaz *et al.*, 1954), but the evidence supports the view that the amines present in arterial extracts are liberated at sympathetic nerve endings bound to the vessel wall (Schmiterlöw, 1948).

The concentration of noradrenaline appears to be greater in the sympathetic nerve endings than in the nerve trunk. It has been stated that in man the sympathetic trunk contains 2–3 microgrammes noradrenaline per gramme of nerve (Euler, 1951). After its release by sympathetic stimulation, the chemical transmitter is rapidly replaced, so that the content is always at a maximum at the nerve terminals (Euler, 1954). It has been shown that if the sympathetic nerves are allowed to degenerate, noradrenaline in an organ disappears but reappears on regeneration.

While noradrenaline is the dominant sympathetic transmitter, it is probably supported by adrenaline, the amount of which is variable, but normally less than 10 per cent of the total amine content of an organ. Some of the adrenaline found in organ extracts may be contained in chromaffin cells, distinct from the sympathetic nerve endings (Euler, 1954).

Noradrenaline and adrenaline are present in the brain (Euler, 1946; Holtz, 1950). They exist in the cerebral vasomotor nerves, and in the tissues of the central nervous system, where the distribution is uneven (Vogt, 1954). The highest concentration, 1 microgramme per gramme of brain tissue, has been found in the hypothalamus. Considerable amounts of noradrenaline have been identified in cerebral gliomas (Bulbring *et al.*, 1953), and in areas of the brain where there are no ganglion cells (Vogt, 1954), showing that synthesis of noradrenaline may occur in tissues which play no part in the transmission of nerve impulses. It seems inadvisable, therefore, to conclude that cerebral noradrenaline and adrenaline fill a similar role to that played by these catechol amines at sympathetic nerve endings.

ADRENAL MEDULLA

Oliver and Schaefer (1895) showed that the pressor action of adrenal extracts was largely confined to extracts of medulla, which in man comprises about one-tenth of the adrenal gland and shares a common origin with the cells constituting the sympathetic nervous system. Estimations of adrenaline and noradrenaline in the adrenal medulla of patients who have died in hospital have yielded average figures of 1.26 mg and 0.21 mg per gramme respectively, i.e. a noradrenaline content of approximately 15 per cent. In the cortex, which contains both amines, noradrenaline comprised 3 per cent of the total content of 0.112 mg per gramme (Shepherd and West, 1951).

The sympathetic fibres to the adrenal medulla are preganglionic in type, liberating acetyl choline, which is present in adrenal venous blood (Feldberg *et al.*, 1934).

In different animals, the relative amounts of adrenaline and noradrenaline vary widely although they appear to be quite constant for each species.

The only other medullary component known to be present in considerable quantities is ascorbic acid, thought to be concerned with maintaining the two hormones in a stable, reduced state (Euler, 1951). Hydroxytyramine (Shepherd and West, 1953) and, more recently, an isoprenaline-like substance (Lockett, 1954) have been found in extracts of medulla, but their importance is not established.

Adrenaline and noradrenaline occur in microspheres, or presecretory granules, within the chromaffin cells of the medulla (Welch and Blashko, 1953). The recognition of the existence of two distinct medullary cell types (Eranko, 1951) led Hillarp and Hökfelt (1953), who confirmed the finding, to offer the following opinion. " All the cells can form noradrenaline, while only certain specific cells—whose number varies from none to all of the medullary cells in various animals—are able to effect a mechanism for the methylation of noradrenaline to adrenaline and store this hormone. Those cells which lack this methylation capacity store noradrenaline."

At birth the adrenal glands and other chromaffin tissues, e.g. the organs of Zuckerkandl, contain predominantly noradrenaline (Shepherd and West, 1951; West *et al.*, 1953). By the age of seven months, the proportion of noradrenaline is about one-half that at birth, and at two and a half years, the content has fallen to 32 per cent (Shepherd and West, 1951). It has been shown that adrenal extracts (Bulbring, 1949) and the isolated adrenal gland of the dog (Bulbring and Burn, 1949) can form adrenaline from noradrenaline by methylation, and the suggestion has been put forward that from infancy to adulthood there is a progressive increase in the number of special methylating cells. It is of interest that while in man the normal content of noradrenaline in the medullary secretion is below 20 per cent, the secretion from tumours of the medulla contains predominantly noradrenaline. Tumour tissue appears to resemble the embryonic gland in its inability to methylate noradrenaline. While there is suggestive evidence that noradrenaline is the precursor of adrenaline, the process of methylation may not be easily accomplished after depletion of the gland (Udenfriend, 1953).

Available evidence points to the existence of a normal continuous " resting " secretion of adrenaline and noradrenaline from the adrenal medulla. The figure of 0.03–0.06 microgramme per kg per minute is quoted for the basal discharge of adrenaline from the two adrenal glands in cats and dogs (Kaindl and Euler, 1951; Dunér, 1953; Houssay and Rapela, 1953; Wada and Kanowoka, 1935). It must be stressed, however, that the secretion may be quite drastically altered by the various procedures employed in animal experiments.

Although it is probable that the relative proportions of adrenaline and noradrenaline in the medullary secretion are dependent on the nature of the stimulus and the functional effect required, the evidence for this is incomplete. An established finding, however, is the release of adrenaline during the hypoglycaemia induced by insulin (Dunér, 1953; Euler and Luft, 1951; Hökfelt, 1951; Outschoorn, 1952; Holzbauer and Vogt, 1954). The opinion held by Hillarp and Hökfelt, that by means of selective innervation either amine can be secreted from the medulla alone or both together, is supported by the finding that direct hypothalamic stimulation releases either adrenaline or noradrenaline depending on the site of stimulation (Folkow and Euler, 1953). Adrenaline, the " emergency hormone " of Cannon, appears to be primarily concerned in the regulation of certain metabolic functions. It has been stated that under conditions involving circulatory stress, the hormone selectively released is noradrenaline (Euler, 1954).

INACTIVATION AND EXCRETION OF CATECHOL AMINES

At present, while it is considered that the removal of noradrenaline and adrenaline occurs by enzymatic inactivation, the role played by the two enzymes, catechol and amine oxidase, is not clearly established.

Amine oxidase is widely distributed in organs, glands, brain and nerve tissue (Blashko, 1952). It is present in the adrenal cortex and medulla (Langemann, 1951), it has been found in blood vessels (Thompson and Tickner, 1951), and it has been extensively identified in areas innervated by sympathetic nerves. However, certain facts are difficult to reconcile with the view that amine oxidase is the specific inactivator of noradrenaline and adrenaline at sympathetic nerve-endings. The high concentration of the enzyme in liver and kidney—considerably higher than in the adrenal medulla—has not been explained; other enzymes,

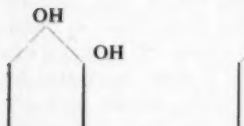
e.g. tyramine, hydroxytyramine, and 5-hydroxytryptamine (serotonin, enteramine, thrombocytin), are more rapidly oxidized by amine oxidase *in vitro* than is noradrenaline (Blashko, 1952); also, the enzyme has been found in the placenta, which is nerve-free and contains no catechol amines (Thompson and Tickner, 1949).

It has been stated that destruction of amines liberated into the blood from sympathetic nerve endings, or from the adrenal medulla, takes place largely in the kidney (Bacq, 1937). Inactivation occurs by conjugation, the products being excreted in the urine as ethereal sulphates or glucuronides (Euler, 1951). Small amounts are excreted in the free form.

Holtz *et al.* (1947) found that urine normally contained sympathomimetic substances, considered to be a mixture of adrenaline, noradrenaline, and hydroxytyramine, and given the collective name " urosympathin ".

Human urine normally contains up to 60 microgrammes noradrenaline and 9 microgrammes adrenaline in 24 hours (Euler, 1954). The relative proportion of the two amines suggests that the normal output is derived mainly from adrenergic nerve mediators (Goldenberg and Rapport, 1951). From infusion experiments it is evident that only a small fraction of the amounts present in the blood appear in urine. Recovery of infused noradrenaline was found to be 1.5–3.3 per cent (Euler and Luft, 1951), while only 0.36–1.65 per cent of infused adrenaline could be detected in urine (Euler *et al.*, 1954). Moderate, although inconsistent, increases in urinary noradrenaline have been reported in hypertensive patients; the existence of adrenal medullary tumors may increase the daily output to a figure in excess of 2 mg (Goldenberg, 1954).

CHEMISTRY

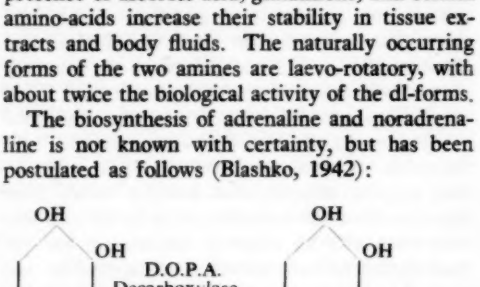


Noradrenaline *Adrenaline*

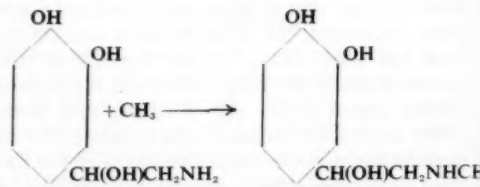
The chemical structure of catechol consists of a benzene ring with two adjacent substituted hydroxyl groups. Adrenaline is a secondary catechol amine, containing a CH_3 group in the side chain. The absence of this methyl group in noradrenaline (which is a primary catechol amine) is indicated by the prefix " nor "—" N ohne Radikal "—nitrogen without the (CH_3) radical.

Adrenaline and noradrenaline are easily oxidized, especially in alkaline solution, but the presence of ascorbic acid, glutathione, and certain amino-acids increase their stability in tissue extracts and body fluids. The naturally occurring forms of the two amines are laevo-rotatory, with about twice the biological activity of the dl-forms.

The biosynthesis of adrenaline and noradrenaline is not known with certainty, but has been postulated as follows (Blashko, 1942):



(D.O.P.A.)
Dihydroxyphenylalanine *Hydroxytyramine*
[From Tyrosine or Phenylalanine]



Noradrenaline *Adrenaline*

Although the enzyme D.O.P.A. decarboxylase has been found in various animal tissues including the adrenal medulla (Langemann, 1951), and in the human kidney (Blashko, 1942), the existence of D.O.P.A. has not been demonstrated. Hydroxytyramine has been identified in extracts of mammalian heart and adrenal glands (Shepherd and West, 1953), and is present in human urine (Holtz *et al.*, 1947; Euler and Hellner, 1951).

ESTIMATION IN BLOOD

The estimation of adrenaline and noradrenaline in blood has presented great difficulties, mainly due to the very small amounts which are normally

present. Chemical methods of assaying the two amines in mixtures have usually lacked adequate sensitivity and specificity, while biological methods, although often quite sensitive, have tended to be inaccurate. Recently the use of paper chromatography (James, 1948), and the development of methods of parallel quantitative assay—using the rat's blood pressure for noradrenaline (Crawford and Outschoorn, 1951) and the rat's uterus for adrenaline (Gaddum and Lembeck, 1949)—have increased sensitivity and allowed the estimation of normal plasma samples by biological methods. The technique is difficult, however, and unless it is further developed must remain a formidable and lengthy undertaking except in a few select centres.

Chemical methods for the estimation of catechol amines were based initially on the observation made by Vulpian in 1856, that extracts of adrenal medulla produced a green colour when treated with ferric chloride, and that a red coloration was formed by the addition of iodine and mercuric chloride. Many of the commonly used oxidizing agents can effect the conversion of adrenaline to the red oxidation product, adrenochrome, which is then estimated colorimetrically (Euler and Hamberg, 1949). Other methods were based on the colour formation produced by adrenaline in the presence of heavy metals (Shaw, 1938).

Modern chemical methods of adrenaline and noradrenaline estimation are based on fluorimetric techniques. In the method of Lund (1949a, b, c), adrenaline is oxidized by manganese dioxide (in acid solution) to adrenochrome, which is then converted by alkali (sodium hydroxide) into the fluorescent compound, adrenolutine; however, the sensitivity of the method, as used by Lund, did not allow the measurement of normal plasma levels of adrenaline. The most recent fluorimetric technique makes use of a strong alkali, ethylene diamine, which condenses with adrenaline and noradrenaline to form fluorescent products of unknown chemical structure (Weil-Malherbe and Bone, 1952).

For estimation, a plasma sample is passed through a column of aluminium oxide, on which adrenaline and noradrenaline are adsorbed. The amines are eluted from the column with acetic acid, then condensed with ethylene diamine. The fluorescent compound is extracted into isobutyl alcohol and the fluorescence read on a sensitive photofluorimeter. By using two filters, advantage can be taken of the different fluorescence spectra of adrenaline and noradrenaline, and the use of a simultaneous equation allows the estimation of both amines.

This method has sufficient sensitivity for the estimation of adrenaline and noradrenaline in normal blood, but the figures published by Weil-Malherbe and Bone (1953) for normal peripheral blood levels in human subjects—approximately 5 microgrammes noradrenaline and 1 microgramme adrenaline per litre of plasma—are almost certainly too high. For this and other reasons the method has been justly criticized; however, other workers (Manger *et al.*, 1954; Aronow and Howard, 1955; Valk *et al.*, 1956), have found normal levels to be considerably lower. Recent work suggests that the average normal adrenaline level in human subjects and in dogs at rest is about 0.2 microgramme per litre of plasma (Valk *et al.*, 1956). This is in good agreement with the values obtained by the use of paper chromatography and biological assay (Holzbauer and Vogt, 1954).

With this fluorimetric technique, however, the estimation of noradrenaline is easily affected by spurious factors, which introduce contamination or which behave like noradrenaline; in general, the estimation of this amine appears to be less specific and less satisfactory than the estimation of adrenaline by this method (Valk *et al.*, 1956).

During the course of the next few years, the use of chemical methods for the estimation of adrenaline may bring to light interesting facts concerning the effect of anaesthesia on adrenal medullary secretion, with, it is hoped, some clarification of the current beliefs and concepts on the subject of adrenaline liberation under different physiological and pathological conditions of intimate concern to the anaesthetist.

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STUDIES WITH LOCAL ANAESTHETICS

A Review of the Literature concerning the methods of comparing Local Anaesthetic Properties

BY

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PRIOR to carrying out an investigation into the claims regarding two new local anaesthetics, a survey of the tests used for the comparison of local anaesthetic properties showed none of them to be satisfactory. This does not imply that there has been a lack of interest in developing new methods. On the contrary, in the search for the elusive ideal, large numbers of drugs have been subjected to many varied and ingenious pharmacological tests.

The situation has been summed up by Jenkins and Hartung (1949) who, when discussing the relation between chemical structure and local anaesthetic activity, stated: " unfortunately the evaluation of local anaesthesia was made by as many different procedures as there were investigators, and it will be impossible to summarize completely the effect of chemical structure and physiological activity. To do so would necessitate an attempt to reconcile many conflicting results."

This paper aims at describing briefly some of the recent methods used or proposed for future use. These have been classified according to the three types of anaesthesia required by clinicians:

(1) *Topical anaesthesia*—following surface application of the local anaesthetic to mucous membrane and cornea.

(2) *Conduction anaesthesia*—in which the anaesthetic solutions are brought into intimate contact with nerve trunks.

(3) *Infiltration anaesthesia*—where the local anaesthetic is widely infiltrated into the tissue to be anaesthetized.

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(1) TOPICAL ANAESTHESIA

(a) *Human Tongue.*

This test was the one first used to observe the local activity of the pure crystals of the alkaloid cocaine (Wöhler, 1860). Despite the attempts of Squibb (1885, 1892) to make this test quantitative by applying small squares of filter paper containing known amounts of cocaine to the tongue, this test is useless for the comparison of activity. Many compounds which have only slight irritant but no anaesthetic properties give the impression of loss of sensation on the tongue.

(b) *Frog's Skin.*

Local anaesthetics penetrate frog's skin, for it possesses many properties of mucous membranes. Sollman (1918a) and Kubota (1919) studied a method of stimulating the frog's leg with N/10 HCl following its immersion in the solution under test. Onset of anaesthesia was tested by this means but since no recovery from anaesthesia could be demonstrated, permanent damage and reversible anaesthesia could not be differentiated.

(c) *Laryngeal Reflex.*

An objective method of determining the duration of a topical anaesthetic has recently been described by Clark, Orkin and Rovenstine (1954). This utilizes the laryngeal reflex to mechanical stimulation whilst the patient is under a light plane of anaesthesia. The main advantage of such a procedure is that the reflex is not influenced by the emotional state of the individual, or by variations in pain threshold among subjects. It is claimed that this test can be used better than any other to predict the duration of effective anaesthesia which a drug will produce for endoscopic examinations.

(d) *Mammalian Cornea.*

A degree of dependability characterizes the method using the mammalian cornea which aims at measuring the ability of a compound to penetrate and paralyse the superficial sensory endings of the cornea. There seems to be general agreement that the cornea, at least in its central area, possesses one type of surface reception. This should be regarded as nociceptive although in various respects it is distinct from the corresponding sensation in the skin (Björk, 1950).

Sollman (1918b) described a procedure which has served as a model for much of the later work. He clipped the lashes of the rabbit which was placed in an individual stall with its head free. The lower lid was pinched into a pocket into which was inserted the local anaesthetic solution which was kept in contact with the cornea for exactly one minute. The eyelid was released and after ten minutes the centre of the cornea was stimulated with the tip of a lead pencil. If no winking resulted the pencil was drawn across the cornea several times with moderate pressure. If, however, winking showed that anaesthesia was absent a further application of the solution was made. The tests and applications were repeated at ten-minute intervals.

Sollman aimed at finding the minimal effective concentration and it is interesting to note that for procaine to be effective an 8 per cent solution required to be applied twice.

Variations in the performance of this test have been numerous and the following is a summary of the different techniques claimed to be important.

(i) Duration of contact of the local anaesthetic solution. This has varied from a minimum of two seconds (Chance and Lobstein, 1944) to five minutes (Sinha, 1936).

(ii) pH of solution. The majority of workers have simply dissolved the hydrochloride of the local anaesthetic in distilled water and as a result the effect on the cornea cannot be compared to that when the solution is injected into tissue endowed with considerable buffering properties. Since variation of pH can materially alter the duration of anaesthesia on the rabbit cornea (Evans and Geddes) it is essential to standardize the pH by dissolving the anaesthetic in buffered solutions.

(iii) The application of the minimum effective concentration (Trevan and Boock, 1927) as opposed to fixed concentrations and plotting the duration of anaesthesia. Regnier (1929) in an investigation of the corneal test to assay unknown concentrations of solutions claimed an accuracy of 20 per cent, but this was only when concentrated solutions were used. Thus investigators estimating minimal effective concentrations can hardly hope for accurate results.

(iv) Method of stimulation. Sollman (1918b) varied the intensity of the stimulus by drawing the pencil point across the cornea to determine partial anaesthesia. Regnier (1923), using a hair, claimed to be able to differentiate different degrees of anaesthesia by the number of stimuli required to elicit blinking. If 100 taps did not produce this result, anaesthesia was complete. Chance and Lobstein (1944) simplified Regnier's method and applied stimuli to the cornea every minute, recording the numbers of stimuli which failed to arouse a blink reflex. Burn (1946–47) hailed this as a valuable aid to the problem of testing local anaesthetics. Rose (1929) recommended the use of electrical stimuli by means of faradic current, claiming that by varying the intensity of the current required to elicit the blink reflex it was possible to plot the depth as well as the duration of anaesthesia. An electric spark discharge from a small 4-volt Oudin high-frequency coil was employed by Molitor and Robinson (1938).

A novel stimulus was a standard puff of air released at a fixed distance from the cornea, as suggested by Goldberg (1943), but so far no full-scale investigation has been carried out using this method. It is, however, deemed worthy of trial for it has the advantage of being the least traumatic to the surface of the cornea yet giving rise to a stimulus of considerable intensity.

(v) Choice of animal. The rabbit has been used by the majority of the workers for the corneal test, though a minority (McIntosh and Work, 1941; Chance and Lobstein, 1944) favour the guinea-pig. The latter cannot be recommended, however, for their eyes are too small to permit accurate testing. Even in rabbits there are marked individual variations, and Meeker (1925) noted that there were some rabbits which would tolerate

stimulation when no anaesthesia was present, whereas others, usually those resisting handling, would blink prematurely.

(vi) Variation between right and left corneas. Regnier's 1929 experiments demonstrated that the right and left eyes may have different durations of anaesthesia for the same dose of the same anaesthetic. Thus authors who use one eye for the control and the other for the unknown solution do not have a true standard for comparison. Regnier recommends that each eye be treated as a single experiment and by the accumulation of sufficient data the average results can be analysed.

(vii) Human experiments. Björk (1950), who performed corneal tests, as did Marx (1924), on the human cornea, comments on the selection of volunteers. A number of individuals became fatigued and following partial return of sensation there was a further period of anaesthesia which continued for some time. Björk (1950) also recommended applying the stimuli in a circle parallel to the limbus in order to avoid possible damage to the centre of the cornea.

Summary.

It will be seen from the foregoing that apart from the use of the laryngeal reflex in man the rabbit cornea is the test most likely to be of value when comparing the topical potency of a new local anaesthetic. From a practical point of view it is extremely difficult to decide accurately whether an eye is anaesthetized or not. If this test is to be used the procedure should be standardized and sufficient experiments should be performed to allow statistical appraisal of the results to be carried out.

(2) CONDUCTION ANAESTHESIA

The use of nerve trunks is complicated by the fact that they contain many fibres of different diameter, and in animal experiments the duration of sensory anaesthesia is difficult to determine due to the lack of criteria for sensory discrimination. Whether it is justifiable to use motor block as a criteria for anaesthesia of sensory nerves is a debatable point.

(a) *Sciatic Nerve.*

(i) Frog. Mommsen (1881) was the first to use the sciatic nerve to demonstrate local anaesthetic activity and there are numerous other descriptions of the successful use of this preparation: Sollman, 1917; Bulbring and Wajda, 1945; Ehrenberg, 1948; Brown and Luduena, 1953; the latter authors reported that they were able to demonstrate recovery of conduction following block even after 4–6 hours in the case of one compound tested. Rider (1930) noted a marked variation in the individual frogs, especially a seasonal variation in the spring and autumn frogs. Regnier (1929) concluded that the variations of the different preparations greatly exceeded the variation resulting from the different concentrations.

(ii) Rabbit. The sciatic nerve of rabbits has been exposed under ether anaesthesia, and following stimulation general effects such as raised blood pressure and alteration of respiratory pattern were noted. Local anaesthetic solutions were painted on the nerve and following stimulation the onset of anaesthesia was determined by the absence of the general reactions. Dixon (1905) and Schmitz and Loevenhart (1925) used this method, although no attempt was made to determine the duration of anaesthesia. The crossed sciatic reflex has been used by Van Leeuven and Verzar (1923) to demonstrate the onset and duration of anaesthesia in the decerebrated rabbit. The technical difficulties of this preparation unfortunately limit its use.

(iii) Guinea-pig (*in situ*). This is an attempt to use the procedure of nerve block to permit the comparison of local anaesthetic potency. The sciatic nerve is blocked where it lies beneath the trochanter of the femur and the vertebral column in a short furrow filled with muscular tissue. It can readily be demonstrated by the injection of a dye that it is easy to place the solution in close proximity to the nerve. Shackell (1935) described an area of anaesthesia 2–3 sq.cm in extent on the posterior or lateral surfaces of the thigh or leg. This area of skin was located by pinching with mouse toothed forceps. Unfortunately in many cases difficulty was experienced in locating this area of skin, and Loomis and Spielmeyer (1946) claim that a more reliable criterion of anaesthesia was motor paralysis, when the leg became extended on the thigh in locomotion. This test has been used successfully by Luduena and Hoppe (1952).

(b) *Lingual Reflex.*

An interesting but little used method is that described by Cordot and Laugier (1922) employing the "reflex linguo maxillaire". This consists of the depression of the jaw of a dog following stimulation of the tongue whilst the dog is under chloralose anaesthesia. The reflex path is by the lingual nerve which is exposed and blocked and the inferior maxillary nerve which conveys the motor impulse to the posterior belly of the digastric. Regnier (1929) investigated this reflex but was unable to measure duration of anaesthesia with it.

(c) *Isolated Nerve.*

Bennett, Wagner and McIntyre (1942) and Bennett and Chinburg (1946) described a method of recording the effect of local anaesthetics upon isolated frog sciatic nerves as indicated by the changes in the alpha wave of the action potential. Though it has been claimed to be the ideal method of comparing local anaesthetics, its use has not been widely adopted by other workers.

(d) *Spinal Anaesthesia.*

In an attempt to eliminate outside influences such as penetration of nerve sheath and diffusion, local anaesthetics have been applied direct to the bare nerve tissue by subdural injection.

Early workers used decapitated frogs but Bieter, Harvey and Burgess (1932) used intact frogs. The injection was through a hypodermic needle pointing caudally into the urostyl canal parallel with its axis. The presence or absence of a reflex when the frog's legs were immersed in 0.5 per cent hydrochloric acid was taken as the criterion of anaesthesia.

Shackell (1937) used spinal block in the rat and Bieter, Cunningham, Lenz and McNearney (1936) extended this test to the rabbit. After numerous experiments the volume of fluid injected which gave no intradural pressure rise was found to be 0.02 ml per cm of spinal length. Following injection of the local anaesthetic solutions through the intervertebral space at the lumbosacral union, sensory paralysis was tested for by means of an induction coil and the effect on respiration observed. The minimum effective concentration and duration of anaesthesia were noted.

Luduena and Hoppe (1951) used the same technique as Bieter *et al.* in rabbits but criticized the difficulty in accurately determining the duration of anaesthesia, as this wears off gradually. In their opinion the best end point was given by the "urethral reflex". This reflex consisted of a contraction of the sphincter ani externus following the intra-urethral injection of cold water.

Summary.

Of the tests for conduction anaesthesia, the most logical would appear to be Shackell's test, but unfortunately in practice it is often very difficult to determine the duration of the anaesthesia even when motor block is used as a basis for comparison.

(3) INFILTRATION ANAESTHESIA

This method of comparing local anaesthetic solutions is that most closely analogous to clinical usage. It comprises two main methods, subcutaneous and intradermal.

(a) *Subcutaneous.*

Following subcutaneous injection of the local anaesthetic solution the area of anaesthesia produced is tested for by absence of reaction to stimuli and its duration noted. Tests of this nature have been carried out in the dog (Pittinger, 1921; Moxon and Pawlisch, 1925).

Infiltration of the subcutaneous tissues about the external canthus of the rabbit's eye was used by Tatum (1931). Anaesthesia was tested for by abolition of the lid reflex when the lashes of the upper lid were touched with a probe. Lesser (1940) used a subconjunctival injection of the local anaesthetic, a method used first by Labord (1884) with cocaine. Luduena and Hoppe (1951) are recent workers using this test.

Herr, Nyiri and Pataky (1953) and Mack and Nelon (1953) described a method of subcutaneous infiltration at the base of a rat's tail and subsequent stimulation by radiant heat using the apparatus described by Hardy, Wolff and Goodell (1940). The progress of anaesthesia was plotted and a linear relationship was claimed between concentration and duration of anaesthesia. A grave disadvantage of this method is that thermal damage may occur when seeking return of sensation.

Gordh (1949) in experiments on man reported the duration of anaesthesia following subcutaneous infiltration of 1 ml of lignocaine. However, following subcutaneous injection it is difficult to standardize the depth of injection and a constant nerve supply cannot be guaranteed, even in closely related areas and this makes accurate comparisons difficult.

(b) *Intra-oral.*

Björn (1946) constructed an electric pulp stimulator and used it to determine the efficiency of local anaesthetics employed in dentistry (Björn, 1947). The pain threshold to electrical stimulation was first plotted; then, following the injection of the local anaesthetic, the progress of anaesthesia could be followed. The efficiency parameters utilized were frequency, extent, and latency of anaesthesia obtained (Björn and Huldt, 1947). Calculation of latency and duration of anaesthesia was, however, difficult on occasions. Not infrequently after the occurrence of complete anaesthesia the sensitivity of a tooth returned for a short interval and then disappeared.

The main difficulty of this method is to obtain suitable electrodes to ensure that the measured current is really reaching the teeth. Björn (1946) notes that merely exhaling moist air can materially alter the resistance and thus give rise to an altered threshold. However, this method of assessment, despite the technical difficulties, would appear to be of greater value than some of the tests used by pharmacologists to compare local anaesthetics.

(c) *Intradermal Tests.*

(i) Guinea-pigs. Rose (1929) first described a method of comparing local anaesthetics by intradermal injections in guinea-pigs, 0.1 ml of solution being injected. The stimulus was by means of an induction coil, the current used being that which, when applied to an unanaesthetized area on the guinea-pig's back, was just sufficient to cause the animal to move. It was demonstrated that the duration of anaesthesia was proportional to the differences in concentration of anaesthetics.

McIntyre and Sievers (1937), however, believed that the guinea-pigs could become conditioned to the sound of the contact breaker of the inductorium. For this reason they preferred to stimulate the area with a light pinch, but complained of the difficulties in evaluating the reactions of the animals to pain.

Bulbring and Wajda (1945) applied the method of repeated stimuli which was proposed by Chance and Lobstein (1944) for the corneal test, and stimulated the area injected for anaesthesia six times at regular intervals.

Somers and Edge (1947) observed that a considerable variation existed in the sensitivity of the various regions of the back of guinea-pigs, and that significant differences existed between the responses of the same animal on different days. In order to reduce these errors the experiments were specially designed in the form of a latin square. Three solutions were tested simultaneously in three positions chosen in line on the backs of three guinea-pigs. The three drugs were injected at three dose levels over three successive days. All compounds were injected with the same dose level on any one day, during which three half-hour comparisons were made. Thus, each animal received each drug, but in different positions. Since each latin square was a 3×3 design, the total number of squares 9, and the total number of guinea-pigs 9, the results were based on 81 individual comparisons. The number of failures to elicit a response to painful stimulation of the anaesthetized areas was noted over a period of 30 minutes and by plotting this against the logarithm of the concentration of the drug used, a linear relationship was established. Goldberg (1949) in a much larger series of randomized tests confirmed the variation between animals, and a smaller variation in different positions on the same animal.

The design of tests to compare local anaesthetics so that the results can be analysed statistically is the only logical approach to the problem where so many variable factors have been shown to influence the results.

(ii) Man. The solution to be tested is injected between the layers of the skin so that a visible weal is raised; if the injection is correctly made the follicles of the hair are easily visible. The size of the weal depends upon the volume of solution injected and the depth of the injection. Sollman (1918c) states that the exact size and the quantity injected are immaterial. For purposes of compari-

son it is considered desirable that fixed amounts of solution should be injected and when performing this test precautions should be taken to use only syringes that do not leak and a fine 26 gauge short bevel needle helps accurate deposition of the solution.

(iii) Cantharidine blister. The sensory nerve endings can be exposed by removing the epidermis by the use of a cantharidine plaster. Local anaesthetic solutions can then be applied directly and anaesthesia can be tested for by either a needle (Bert, 1885) or the use of a spring loaded camelhair brush (Mongar, 1955). The duration of anaesthesia is not measured, but it is claimed that by applying various concentrations of solutions, different degrees of anaesthesia can be distinguished and used to compare the activity of different anaesthetics.

Summary.

The intradermal method of testing for duration of anaesthesia, especially when performed on human volunteers on a scale which permits the statistical appraisal of results, is more reliable than the use of animals.

CONCLUSIONS

From this survey of the multitude of methods used by investigators to compare local anaesthetic efficiency of new drugs, the overriding conclusion is that without a standard method of evaluation, the mass of data cannot be correlated. Two drugs cannot be compared accurately unless both compounds have been tested by the same technique and the same worker. In the literature on local anaesthetics the standard of reporting results has been low, a fact which is unhelpful to workers attempting to repeat tests.

The personal factor is continually cropping up, for as each new compound is introduced authors strive to prove its superiority, often by emphasizing relatively unimportant properties. It is also interesting to observe that tests successfully employed by one group of workers are often condemned by others. A possible explanation is that considerable training of both animals and operators is necessary before many tests yield results of value.

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CORRESPONDENCE

USE OF THE HEWER MATTRESS

Sir,—My attention has been drawn to a paper by Dr. Hacker (October, page 495) advocating the interposition of a sheet between the patient's back and the ribbed mattress now known as the "St. Bartholomew's Hospital Pattern" when using the Trendelenburg position. After exhaustive tests I can say quite definitely that this practice is satisfactory for normal patients in moderate degrees of tilt, but that the diminution in the coefficient of friction may allow slip in extreme conditions.

At the same time I might mention that it is quite unnecessary to lift a nude patient from the trolley to the table. The usual practice is to clothe the patient in usual theatre gown, with the back tapes undone, and to place him on a canvas stretcher on the trolley. When anaesthetized he is lifted by the poles on to the operating table, the poles are withdrawn, and he is then turned on to his left side. The stretcher is tucked under him and he is then turned on to his right side and the canvas removed. He now lies on his bare back, and the front of the gown is pulled up as far as is necessary. The forearms are either secured to the rubber straps on the lumbar bolster or folded over the chest as described recently by Sir Robert Macintosh.

This technique involves no more lifting than any other.

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THE ANATOMICAL APPROACH IN STELLATE GANGLION INJECTION

BY

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THE sympathetic outflow to the head and neck and the greater part of that to the upper limbs passes on each side through the relatively small confines of the stellate ganglion and is here subject to interruption by stellate ganglion block.

This block will cut off all efferent sympathetic impulses to the head and neck and most, if not all, of those to the upper limb and may be of value for example in estimating the likely improvement in blood supply that would follow a cervical sympathectomy in Raynaud's or other vascular diseases and also as a therapeutic measure temporarily increasing the blood supply in cerebral thrombosis or embolism pending the opening up of collateral circulation.

In addition certain visceral afferent fibres pass through the stellate ganglion, for example, cardiac pain impulses are believed to pass by the middle and inferior cervical cardiac branches of the sympathetic to the cervical sympathetic trunk and so through the stellate ganglion (Peterson, 1938; Mitchell, 1953). Stellate ganglion block, especially if combined with block of the upper thoracic ganglia of the trunk, may relieve the pain (White, 1940).

The outflow to the head and neck leaves the spinal cord through the first thoracic nerve and passes by the white ramus communicans to the first thoracic or the stellate ganglion of the sympathetic trunk. The fibres turn upwards and after synapse here or in the middle or superior cervical ganglia are distributed by grey rami to the cervical nerves, by communications to the last four cranial nerves, by visceral branches to cervical viscera and to the heart, and by the vertebral and internal carotid nerves to the interior of the cranium.

The outflow to the upper limb leaves the spinal cord through the white rami of the second to the sixth or seventh thoracic nerves (Foerster, 1939). The fibres turn upward and after synapse in the thoracic, stellate, vertebral or middle cervical ganglia pass through grey rami for distribution through the brachial plexus. Kuntz (1927) has shown that there is a frequent though inconstant intrathoracic connection between the second and first thoracic nerves and Kirgis and Kuntz (1942) have demonstrated a similar connection between the third and second thoracic nerves. These connections would allow sympathetic fibres destined for the brachial plexus to leave the sympathetic trunk at the level of the second and third thoracic ganglia and these fibres would not pass through the stellate ganglion. Therefore to be certain of complete sympathetic denervation of the upper limb stellate ganglion block would be insufficient and it would be necessary to block the sympathetic trunk down to the level of the third thoracic ganglion.

THE ANATOMY OF THE STELLATE GANGLION

The stellate ganglion represents the fusion of the inferior cervical and the first thoracic ganglia with sometimes the second thoracic ganglion in addition and is present in about 80 per cent of subjects (Perlow and Vehe, 1935; Mitchell, 1953). Clinically the term " stellate ganglion " is sometimes used to indicate the inferior cervical and first thoracic ganglia whether or not they be fused. The size and shape of the stellate ganglion are irregular. It varies from 1 to 3 cm in length and from 3 to 10 mm in width (Perlow and Vehe, 1935) but its numerous branches give it a star-shaped appearance. It is often irregularly constricted. It lies in front of the junction of the seventh cervical transverse process with the body of the vertebra, overlapping the longus cervicis to the covering fascia of which it is attached. Around it lie loose areolar and adipose tissue. Traced downwards it lies in front of the eighth cervical nerve,

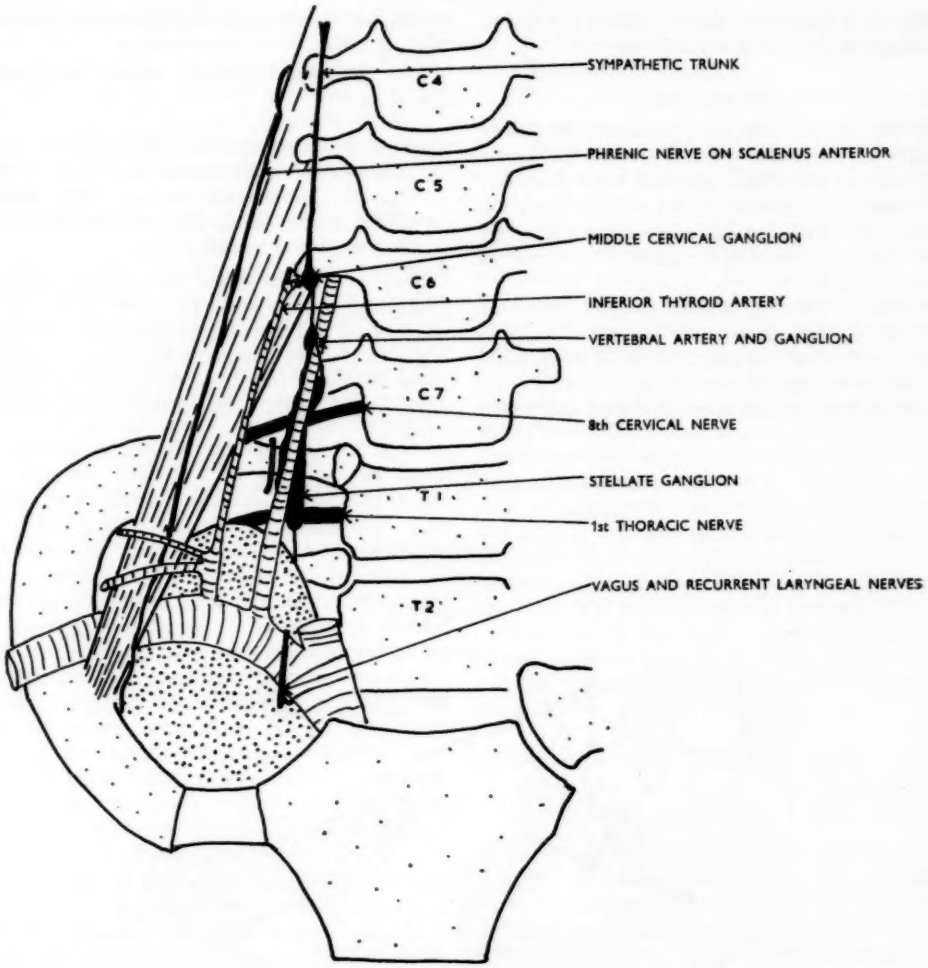

FIG. 1

Schematic view of the thoracic inlet from above and in front.

the neck of the first rib and the first thoracic nerve. Diverticula of the subarachnoid space may emerge with these nerves for a short distance.

Its anterior relations are the vertebral artery and the subclavian artery though this latter is not directly related, while below and in front is the apex of the lung separated by pleura and supra-pleural membrane. The apex of the lung rises to the level of the neck of the first rib or ½ inch to 1 inch above the medial third of the clavicle (Cunningham, 1951).

The common carotid artery, internal jugular vein and vagus nerve are indirect anterior relations; the phrenic nerve on the scalenus anterior is anterolateral; the trachea and thyroid gland, the oesophagus and recurrent laryngeal nerve are anteromedial. The blood supply of the ganglion is obtained from the superior intercostal artery

which is an immediate lateral relation in front of the neck of the first rib (Patterson, 1953).

APPROACHES

It will be seen that the sympathetic trunk lies deeply in the neck, that an anterior or lateral approach to the stellate ganglion must pass close to important structures in the root of the neck, while a posterior approach is less direct and longer and must pass through the plane of the brachial plexus (Fig. 2).

When performing stellate ganglion block no attempt is made at injecting the actual ganglion but a quantity of anaesthetic is placed in the plane in which the ganglion or its equivalent lies and the fluid then diffuses to levels as high as the fifth cervical and as low as the fourth thoracic vertebra (Moore, 1954).

The following approach routes have been employed:

(1) *Anterior or paratracheal* (Orkin, Papper and Rovenstine, 1950; Aymes and Perry, 1950; Adriani, Parmley and Oschner, 1952; Davis, 1952; White, Smithwick and Simeone, 1952; Moore, 1954; Smith, 1951).

This route passes lateral to the trachea and thyroid gland and medial to the great vessels. It is the shortest and most direct approach. Although it passes close to important structures it appears to be relatively free from serious complications (Orkin *et al.*, 1950). In Moore's series of over

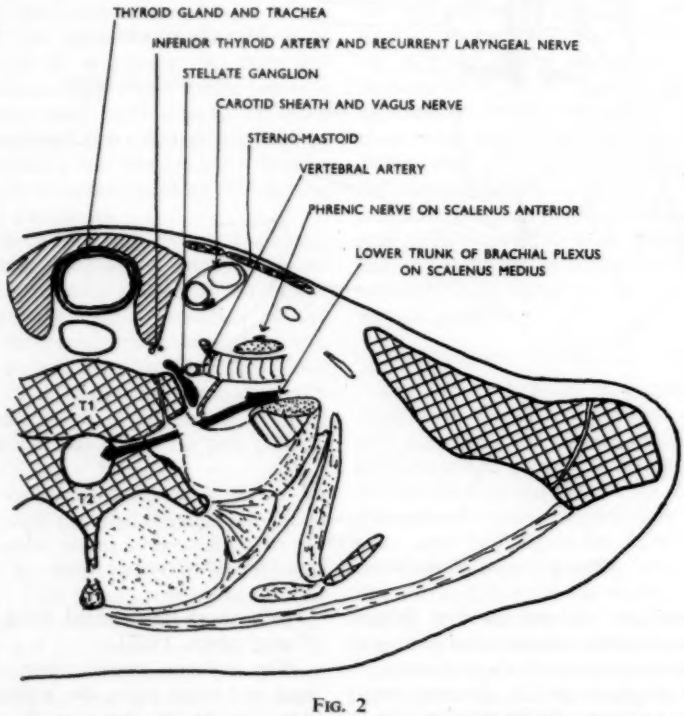

FIG. 2

Drawing made to scale from actual specimen, but modified to show the outline of the first rib, a portion of which occupied a slightly higher plane. Anteriorly the level of the section is ¼ inch above the clavicle, and posteriorly it passes through the tip of the first thoracic spine.
Note the relations of the stellate ganglion and its relative distance from the surface in the various approaches.

2,000 injections using this approach complications were limited to nausea and vomiting from intravascular injections, occasional hoarseness from overflow on to the recurrent laryngeal nerve and partial paralysis of the upper extremity from overflow on to the brachial plexus, complications which are not serious when short-acting drugs are employed.

The technique (Moore, 1954) is as follows: the patient lies in the dorsal recumbent position without a pillow and with the neck in maximum extension in order to straighten the oesophagus. The site of skin puncture is marked at two fingers' breadth lateral to the jugular notch of the sternum and two fingers' breadth above the clavicle. This point should be at the level of the seventh cervical transverse process and is checked by feeling for Chassaignac's tubercle after turning the head to the opposite side, and by marking the lower border of the cricoid cartilage. The point should be about $\frac{1}{2}$ inch below these landmarks. The sternomastoid and the carotid sheath are displaced laterally out of the way, the pulsations of the common carotid being felt on the lateral side of the depressing fingers. The needle is inserted and pushed posteriorly until it impinges on the seventh cervical transverse process at a depth usually not greater than $1\frac{1}{2}$ inch. If bone is not met and paraesthesiae of the brachial plexus are elicited the needle must be withdrawn and directed more medially or slightly upwards or downwards, but this is seldom necessary. After meeting the transverse process the needle is withdrawn $\frac{1}{8}$ inch to free it from muscle.

The needle is aspirated to exclude the possibility that its tip might be in a vessel and as a double precaution a pause of 15 to 30 seconds is made after the injection of the first 2 ml of anaesthetic. Injection into the vertebral artery is dangerous since it directly vascularizes the hind brain and cerebellum. Although it is likely that the needle sometimes passes through the thyroid gland, no sequelae from this cause have been noted.

(2) *Antero-lateral and Lateral* (Leriche and Fontaine, 1934; Goinard, 1936; Arnulf, 1938, 1947; Oschner and De Bakey, 1939; Murphey, 1944; Volpitto and Risteen, 1944; De Souza Pereira, 1945; Fitzpatrick and Higdon, 1946; Clark and Wolfson, 1948; Gilbert and de Takats, 1948; Swan and McGowan, 1951; Bryce-Smith, 1952).

This route begins more laterally at a variable height above the clavicle and passes posterolaterally to the carotid sheath and above the subclavian artery and apex of the lung. Accidental spinal anaesthesia has occurred more frequently with this route than with others (Orkin *et al.*, 1950) and this would be expected as the needle is directed towards the intervertebral foramina. Pneumothorax has also occurred when using this route. De Souza Pereira (1945) in an attempt to avoid these accidents, and to block the middle cervical and vertebral ganglia at the same time as the stellate ganglion, used descending infiltration anaesthesia. He adopts a bony reference point which is easy to find, the anterior tubercle of the sixth cervical transverse process. The soft structures are displaced as far as possible to the opposite side of the neck so that the needle can be introduced in an anteroposterior direction towards the base of this process. This direction prevents the entry into an intervertebral foramen. When pressure on the structures is released the needle assumes a lateral position. Anaesthetic is injected into the prevertebral muscles and into the loose fascia in front of them.

(3) *Posterior or Paravertebral* (Labat, 1930; Wertheimer and Trillat, 1936; Paraf and Le Foyer, 1937; White, 1940; Mandl, 1947).

This route passes through the mass of postvertebral muscles, then between the vertebral transverse processes and close to the emerging spinal nerve and perhaps a diverticulum of the subarachnoid space. The direction of the needle is then changed and it follows the side of the body of the vertebra to the region of the head of the rib. Needles as they advance alongside the bodies of upper thoracic vertebrae are very close to the mediastinal pleura. The route is about $3\frac{1}{2}$ inches (8.8 cm) long, rather more than twice the length of the anterior approach, and it cannot be easy for the beginner to judge the position of the tip of the needle.

The technique (White, 1940) is as follows:

The patient lies on his side with legs drawn up, head flexed and supported so that there is no

lateral curvature of the spine. 10 cm needles are inserted 4 cm lateral to the tip of the seventh cervical spine and upper three thoracic spines. These sites should be at the levels of the upper four thoracic transverse processes. The needles are pushed inward perpendicularly to the skin until the transverse process or the articulating portion of rib is touched at a depth of 2 to 5 cm. It is important to visualize the depth of the ribs in order not to penetrate pleura and puncture the lung. Once contact has been made with the bone the needle is manipulated caudad until it touches the lower border of the transverse process. The depth marker is set at 3 cm from the skin and each needle is now inclined at an angle of approximately 20° with the median sagittal plane. Contact should be made with the side of the body at the further depth of 3 cm and the angle may need to be adjusted to allow this. The needle may be worked forward in contact with the vertebral body. The farther forward the tips of the needles can be inserted and still maintain their contact with bone the less alcohol will come in contact with the intercostal nerves. The needles should not be attached to the syringe during their insertion. The operator must be satisfied that the tips are not within the pleura, within a blood vessel or in an outward prolongation of the subarachnoid space. The latter is more likely to occur if the needle passes above the transverse process in a cephalad direction. Aspiration must always be carried out before injection. It is advisable to inject 2 ml of 2 per cent procaine initially and wait for 5 to 10 minutes. One should be satisfied before injecting alcohol that the needles are placed correctly and that there is no ulnar block.

COMPLICATIONS

Complications may be due to the drug employed or to the approach adopted. No approach is free from complications and those which have been recorded include:

(1) *Puncture of blood vessel.* This is unimportant in itself, but intravascular injection is a danger despite preliminary aspiration. It may occur with any approach and the vessel concerned may be the vertebral, subclavian, inferior thyroid or, especially in the posterior approach to the upper two thoracic ganglia, the costocervical trunk (White, 1940).

(2) *Pneumothorax.* The frequency of occurrence is approximately 2 to 4 per cent when all approaches are considered (Moore, 1954) but pneumothorax rarely occurs when the paratracheal approach is used. The air enters the pleural space from the puncture wound of the lung and may accumulate over some hours. Pleural irritation occurs if alcohol is injected into the pleural cavity.

(3) *Subarachnoid tap.* Cerebrospinal fluid may be aspirated, and this is more likely to occur with the anterolateral and posterior approaches. Accidental spinal anaesthesia is the main danger leading to hypotension and bilateral paralysis. Molitch and Wilson (1931) report a case of Brown-Séquard syndrome following alcohol injection by the paravertebral route.

(4) *Block of the recurrent laryngeal nerve* occurs in 5 to 8 per cent of cases and is more likely in the anterior and anterolateral approaches. Moore (1954) prefers the posterior to the paratracheal route if more than 5 ml of alcohol are to be injected.

(5) *Brachial plexus block*, usually shown initially by tingling or numbness of the hand, is due to overflow of the anaesthetic on to the brachial plexus. If alcohol is to be used radiological control of the position of the needle may be advisable.

(6) *Block of the phrenic nerve* is infrequent.

(7) *Puncture of the oesophagus* was reported by Adriani *et al.* (1952).

SUMMARY

The anatomy of the stellate ganglion is described.

The main hazards of anaesthetic block of the ganglion are intravascular injection, spread to the brachial plexus, injection into the subarachnoid space and pneumothorax.

The route chosen will depend on individual preference but the paratracheal route is the shortest and the most free of serious complications. Its disadvantages, if alcohol injection is contemplated, are the not infrequent spread to the recurrent laryngeal nerve and the brachial plexus. The posterior route may be preferable in certain cases as when much alcohol is to be injected and when thoracic ganglia lower than the stellate are also to be blocked.

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DIRECTOR OF THE RESEARCH DEPARTMENT OF ANAESTHETICS of the FACULTY OF ANAESTHETISTS of the ROYAL COLLEGE OF SURGEONS OF ENGLAND

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PRACTICAL APPLICATIONS OF ELECTRONICS IN ANAESTHESIA

BY

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PART I: BASIC PRINCIPLES

IN the last twenty years much has been heard of the art of electronics and its applications in science and technology. Parallel with these developments electronics has had a rapidly increasing field of application in clinical medicine and surgery, and its scope appears at the moment to be almost unlimited.

It is the purpose of this article first to explain briefly the basic principles of electronics and how they are applied, and then to discuss some applications to clinical work which may be of special interest to the anaesthetist. It is hoped that any reader whose acquaintance with the subject is limited may thus be enabled to visualize how electronics could be of further assistance in his own work.

All electronic devices depend for their operation on the fundamental laws of electricity. While the adjective "electronic" has the literal meaning "pertaining to electrons", the word, together with its associated noun "electronics", has a more limited meaning in everyday usage. As is well known, a current of electricity flowing in a metallic conductor consists of a drift of "free" electrons (i.e. electrons which are not firmly bound in atomic orbits) under the influence of a single potential difference (or pressure) applied between the ends of the conductor. The relation between the potential difference and the current is embodied in Ohm's law.

In the thermionic valve, however, the electrons are made to exist in a condition where their motion is much more susceptible to outside influences such as electric fields, other potential differences or currents, etc. This is done by causing the electrons to form a cloud in free space, where they can be attracted or repelled by charged electrodes in the valve. In the transistor, a more recent development, the electrons exist within the crystal lattice of a semi-conductor and there they may readily be influenced by other currents.

In this way a large current (of electrons) may be controlled by a small voltage or current, and thus the primary function of thermionic valves and transistors is that of amplification. For example, the small electrical action potentials accompanying the normal functions of nerves and muscles can be amplified to a level at which they are capable of operating recording apparatus as described later. Associated with these basic electronic devices is usually found a number of ordinary electrical circuits and components such as resistances and inductances, which are necessary for the correct functioning of the amplifier.

Electronic amplifying circuits, however, will perform other functions. For example, if the nature of the amplification is non-linear, the mode of variation, known as the waveform, of the output voltage or current will differ from that of the input. The circuit is then said to "shape" the waveform, and we are unpleasantly aware of this phenomenon when, because of some accidental non-linearity, the output of our domestic radio receiver becomes distorted and unlike the original sound. Alternatively, by causing part of the output voltage of an amplifier to be fed back to the input in a suitable manner the circuit will produce voltages or currents of any desired waveform. These functions will be explained in greater detail later.

So far we have considered the amplification, shaping and production of purely electrical quantities by means of electronic devices. By the incorporation of another sort of component, called

a transducer, the scope of an electronic system may be greatly increased. A transducer is a device which will convert electrical energy to other forms of energy or vice versa. Familiar examples are the microphone, which converts sound into electrical energy, and the electric motor, which produces mechanical from electrical energy. Thus, for example, if we precede an electronic amplifier by a transducer designed to convert pressure into voltage changes, the system will become a very sensitive pressure gauge. Moreover, if the amplified electrical output is then fed into another transducer which will write on a moving strip of paper or photographic film, the pressure changes may be recorded in as permanent a form as desired. Alternatively, the output transducer may be designed to control some function which must depend upon the value of the input pressure. For example, the blood pressure in an artery or vein may be used to control the action of a mechanical pump which is artificially maintaining the flow of blood during surgery. These facilities, of course, depend entirely on the amplification which is obtained from electronic devices and their associated circuits.

The main functions of electronic systems are therefore:

(1) the amplification, shaping, and production of voltage and current waveforms;
(2) the recording or storage of the amplified voltages;
(3) the use of such voltage waveform for control purposes.

In fact there is a very close parallel between electronic apparatus and the nervous system. For example, the sensory organ of the eye acts as a transducer which converts light into electrical energy: this is, in a sense, amplified and shaped by fibres in the optic nerve and finally conveyed to the brain. Here the brain acts also as a transducer, not only presenting the information in a form intelligible to the organism but often also recording the information as an act of memory. Again, waveforms may be produced in the brain and conveyed via a motor nerve to the muscle which acts as a transducer producing mechanical energy. It is unwise, of course, to press the analogy too far, but it has been further found that when two or more systems interact, for example a sensory and a motor link, the dynamics of the electronic and of the living systems are very similar.

Two important properties of electronic systems have not yet been mentioned. In electronic measuring instruments, because of the high degree of amplification available, it can be arranged that the apparatus absorbs negligible power (electrical or otherwise) from the source of the effect being measured. It therefore introduces little disturbance and we may be tolerably sure that the magnitude of the effect observed will be similar in the absence of the measuring apparatus. Moreover, due to the small inertia of the electron the speed of the electronic system is for present purposes limited only by any mechanical components, i.e. transducers, in the system. In practice, it is easy to design apparatus which will follow the fastest changes encountered in biological systems, but for other reasons, as will be explained later, the design of some types of transducer may be difficult.

Thermionic valves.

Although the transistor is being rapidly developed as an alternative to the thermionic valve in some applications, the latter still remains by far the most important electronic device, and it will therefore be treated in some detail.

The operation of the valve depends upon the phenomenon of thermionic emission. At normal temperatures the free electrons in a conductor have insufficient energy to leave the surface of the conductor. If, however, the metal is heated to an appropriate temperature, ranging from dull red to white heat, in an evacuated vessel, the free electrons will be energetic enough to escape into the surrounding space where they form a negative " space charge ". All thermionic valves contain such a conductor, called the cathode, which may be in the form of a heated filament or cylinder of metal.

The diode, as its name implies, contains two electrodes, the emitting cathode and a plate called the anode. This valve has a very important property. If the anode is maintained at a potential positive with respect to the cathode by a battery connected between the two electrodes, the electrons emitted by the cathode will move across

the interelectrode space and strike the anode. These electrons will flow round the external circuit and form the "anode current". If, however, the anode is negative with respect to the cathode, the electrons will be repelled and no current will flow. Thus the diode acts as an automatic one-way device for electric currents, its operation being determined by the difference of potential between its two electrodes. In this respect its action is very similar to that of a one-way valve for liquids, which opens and shuts according to the pressure difference across it.

The uses of the diode are somewhat limited, but the valve is important in two ways. First, because of its one-way action it may be used to convert alternating current into direct. This process is called rectification, and the diode forms the basis of all power supply units, which may be separate or part of other electronic apparatus, and which operate from the alternating current mains and supply direct current for other valves, etc. Second, it is important as the basis of the triode, a device which will perform most of the functions called for in electronic apparatus.

The triode is similar to the diode in construction, but the electron stream in its travel from cathode to anode passes through a third electrode called the grid. This is usually in the form of a helix of fine wire, so that geometrically it allows free passage to the electrons. The flow of electrons, and hence the anode current, however, may be controlled by varying the potential of the grid relative to the cathode. Figure 1 shows a triode connected in a simple circuit to demonstrate its properties, and figure 2 is a graph relating anode current (Ia) to grid voltage (Vg). If the

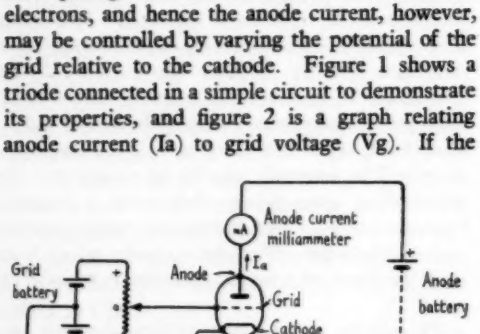


FIG. 1
The triode in a simple demonstration circuit.

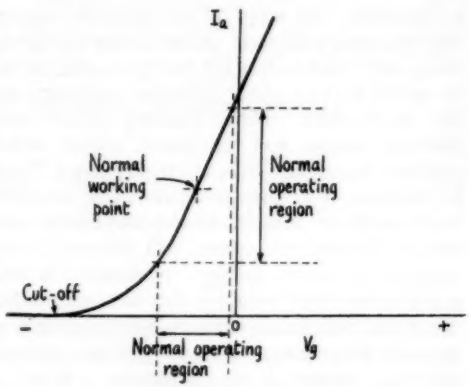


FIG. 2
Characteristic curve of the triode valve.

grid is at cathode potential, its presence has little effect on the anode current. If, however, the grid is made negative, electrons are repelled back to the cathode space charge and the anode current decreases, reaching a value of zero at the "cut-off point". Application of a positive potential to the grid results in increased anode current, because the force of attraction exerted by the grid is added to that of the anode. In this way the anode current, which may be quite large, may be made to vary in sympathy with changes in the grid potential. The triode is therefore the electrical analogue of a non-automatic valve or tap, in which the flow of liquid is controlled by some external influence.

To appreciate fully the value of the triode as an amplifier we must consider further the power expended in grid and anode circuits. In the latter an appreciable current flows at a high potential difference, and hence the output power available is large. In the condition when the grid is negative, it repels electrons, and hence the current flowing in the grid circuit is negligible. For this reason the grid power, which is the input required to operate the valve, is also negligible. It is thus possible to control a large amount of power in the anode circuit by an extremely small power in the grid circuit. Not only does this enable an effect to be amplified, but it does so without reducing its magnitude. For example, a triode amplifier may be connected via suitable electrodes

to a nerve or muscle preparation without disturbing its normal function.

The use of the triode as a power amplifier is shown in figure 3(*a*). The alternator represents

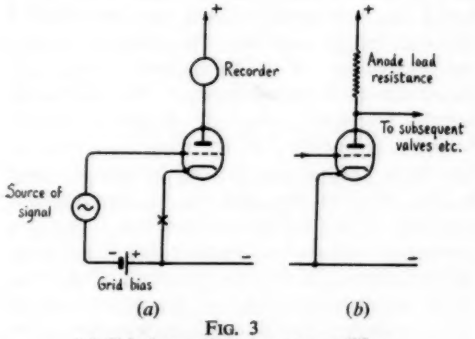


FIG. 3
(*a*) Triode used as power amplifier.
(*b*) Triode used as voltage amplifier.

the source of the effect to be amplified. It is connected between grid and cathode of the valve in series with the battery which serves to set the valve at its correct working point. Clearly voltage variations in the grid circuit will produce corresponding current variations through the recorder in the anode circuit, and the waveform of the variations will be preserved for future reference. Here the recorder in the anode circuit acts as a "load" of low resistance which requires appreciable current but only a small voltage to operate it. At other times, however, the triode amplifier must feed a device of high resistance, such as another valve or a cathode-ray tube. Here high voltage at low current is needed, and this is obtained by allowing the anode current to flow through a high value resistance as in figure 3(*b*). The varying anode current then produces a varying voltage drop across the anode load and this is fed to subsequent valves, etc. Used in this way the triode is behaving as a voltage amplifier, the "gain" of the amplifier being the ratio of output to input voltage change. It is, of course, possible to connect voltage amplifiers together so that the output of one forms the input of the next, and very high values of gain are then possible.

Although the above amplifiers have employed triodes, even more complex valves with extra electrodes are commonly encountered. These are called tetrodes, pentodes, etc., but they will not be discussed specifically as their behaviour is similar in principle to that of the triode.

In the above discussion of the use of the triode as an amplifier it has been assumed that the characteristic curve is linear and unchanging. In practice, however, the characteristic is always curved, and this results in distortion of the output voltage or current waveform. Moreover ageing of the valve and its associated components and alterations in supply voltages cause changes in the performance of the system. It is therefore very desirable to use valves (and transistors) in such a way that the over-all characteristics of the system are substantially independent of such imperfections in the components.

There are two methods of achieving this end, and it is interesting that the human body makes use of very similar methods to stabilize its behaviour and to render it independent of changes in its components. The first is applicable directly to amplifiers, and is known as negative feed-back. In principle it operates by automatically comparing a fixed fraction of the amplifier output with its input, and if any discrepancy exists a correction is made. These operations, of course, occur simultaneously and their speed is limited only by the speed of electrical processes. In a very similar manner, voluntary muscular movements in the body may be inspected visually or otherwise, and the result of the inspection is used by the brain to apply a correction to the original movement if it is inadequate or exaggerated. A very simple way of applying negative feed-back in a valve amplifier is to insert a resistance in the cathode circuit, e.g. at X in figure 3(*a*). If then the anode current of the valve is too large, the cathode will be more positive than normal and this is equivalent to an increase of negative potential on the grid with respect to the cathode. The anode current is therefore reduced. Negative feed-back always results in a reduction of gain, but this is accompanied by an increase in linearity and stability which would be almost impossible to achieve by any other means.

The second method cannot be applied directly to the stabilization of amplifiers. It finds its main application in the conveying of information of one sort or another, and in principle is similar

to the mechanism of nervous conduction, in which a train of impulses of variable frequency characterizes the information to be conveyed. In the electronic analogue valves are used simply as switches, the anode current being turned on and off by making the grid alternately positive and negative. This "valve switch" produces voltage or current pulses, and it is clearly unimportant if the characteristics of the valve change even by a large amount. Radar is a very well-known example of this pulse technique, which is in fact responsible for its great reliability.

We have discussed how valves may be used for linear amplification, but if the characteristic is grossly non-linear the output waveform can differ from the input in almost any desired manner. This is often useful when one type of waveform is available and another is desired.

Valves, however, can also be used for producing specific waveforms. Let us consider a simple triode amplifier with an alternating voltage input producing an output of identical waveform at a much higher energy level. If we simultaneously remove the input and replace it by an identical voltage obtained from the output, the valve would continue to deliver its original output but in the absence of an external input. It is then converting energy from the anode battery into energy of the desired waveform. In practice the waveform so obtained would rapidly degenerate, and it is necessary to have an auxiliary circuit to maintain its shape.

Figure 4 shows a triode arranged to produce a sinusoidal output. The inductance and capacity

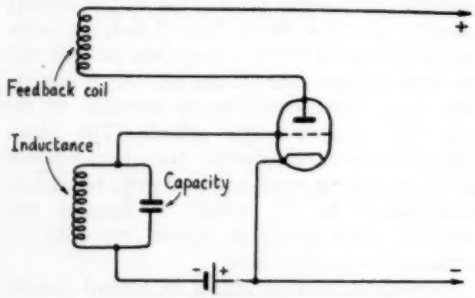


FIG. 4

The triode used to produce alternating currents of sinusoidal waveform.

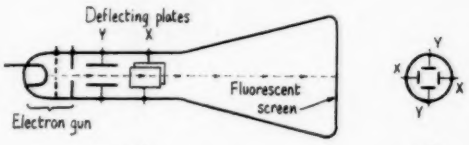
in the input form an oscillatory circuit, which briefly is the electrical analogue of a mechanical vibrating system. Thus if an electrical impulse is given to the circuit, a sinusoidal oscillation will be produced which in the absence of the valve would die away rapidly due to the conversion of electrical energy into heat. In a similar manner the oscillations of a mechanical system will decay due to frictional losses. The alternating voltage produced across the oscillatory circuit, however, is amplified by the triode in a more or less linear fashion, and part of the output energy is fed back to the grid circuit by magnetic coupling. The feed-back in this case is positive, because it is in such a direction that it assists the original input. In this way the energy lost in the input circuit is replaced from the output, and the whole circuit "oscillates" continuously. This basic circuit is used clinically for the production of high frequency alternating currents in "short wave" diathermy.

If, on the other hand, the valve is used merely as a switch, usually in conjunction with a second valve instead of the oscillatory circuit, pulses will be produced. The well-known electronic muscle stimulator operates in this way.

The cathode ray tube.

Before concluding our review of the basic electronic devices and their applications the cathode ray tube must be mentioned as the most important and universally applicable display device. If for example we have a pressure transducer operating into a linear voltage amplifier, the output will consist of a varying voltage, whose waveform is an accurate representation of the original pressure variations. If these variations occur rapidly, as they would in the cardiac cycle, it would be impossible to observe and record them with the unaided senses. The cathode ray tube is a device which will display the waveform as a graph of voltage against time, and the trace so obtained may be viewed, traced or photographed as required. Moreover, the speed of the device is limited only by the inertia of the electrons, which sets an upper limit of the order of several thousand million cycles per second.

Figure 5 shows a cross-section of the cathode ray tube including only the essential features.



(*a*) (*b*)

FIG. 5

(*a*) The cathode ray tube showing essential features only.
(*b*) Cross section of the deflecting system.

Enclosing the whole is a glass bulb flared at one end and thoroughly evacuated. At the small end a heated cathode emits electrons and these are accelerated by an electrode system similar in principle to the triode. The assembly is known as the electron gun, because it produces a beam of electrons which travel down the axis of the tube and strike the end face. This internal surface is coated with a material which fluoresces under the impact of electrons and as a result a small luminous spot is produced which can be viewed from outside. The brightness of the spot may be controlled by varying the potential of the grid in the electron gun. This luminous spot acts as the writing point, and next it must be deflected so as to trace a pattern on the screen. This is done by including two pairs of plates between which the beam must pass, known as the deflector plates. If a potential difference is applied, for example, to the Y plates (see fig. 5(*b*)) the beam will be deflected vertically, i.e. along the Y axis. Similarly a horizontal deflection may be obtained by the use of the X plates.

To examine a voltage waveform the latter (referred to as the signal) is applied to the Y plates and a voltage of saw-tooth waveform to the X plates. The latter causes the spot to move from left to right across the screen at the required speed, and then to fly back rapidly to its starting point. This process may occur periodically if desired. At the same time the signal is producing a vertical deflection, and the result of both processes is the appearance of the desired waveform on the screen. If the X deflection, or time base, is periodic, it can be arranged that successive patterns all coincide on the screen thus giving the illusion of a stationary waveform.

The cathode ray tube possesses similar advantages to the thermionic valve. Its speed is for practical purposes unlimited and as the deflector plates take virtually no current from the source, the waveform observed is a true representation of the original effect.

There are, of course, other methods of displaying and recording waveforms, but as these are not peculiar to electronic systems, they will be dealt with in connection with their special applications.

(To be concluded)

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